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EDITED BY

PAUL C. FREER, M. D., PH. D.

AND

RICHARD P. STRONG, PH. B., M. D.

WITH THE COLLABORATION OF

OSCAR TEAGUE, M. S., M. D.; W. E. MUSGRAVE, M. D.  
VICTOR G. HEISER, M. D.; JOHN R. McDILL, M. D.  
FERNANDO CALDERON, M. D.; JOSÉ ALBERT, M. D.  
PHILIP K. GILMAN, A. B., M. D.; NELLIE LOUISE COOK, B. L., M. A.

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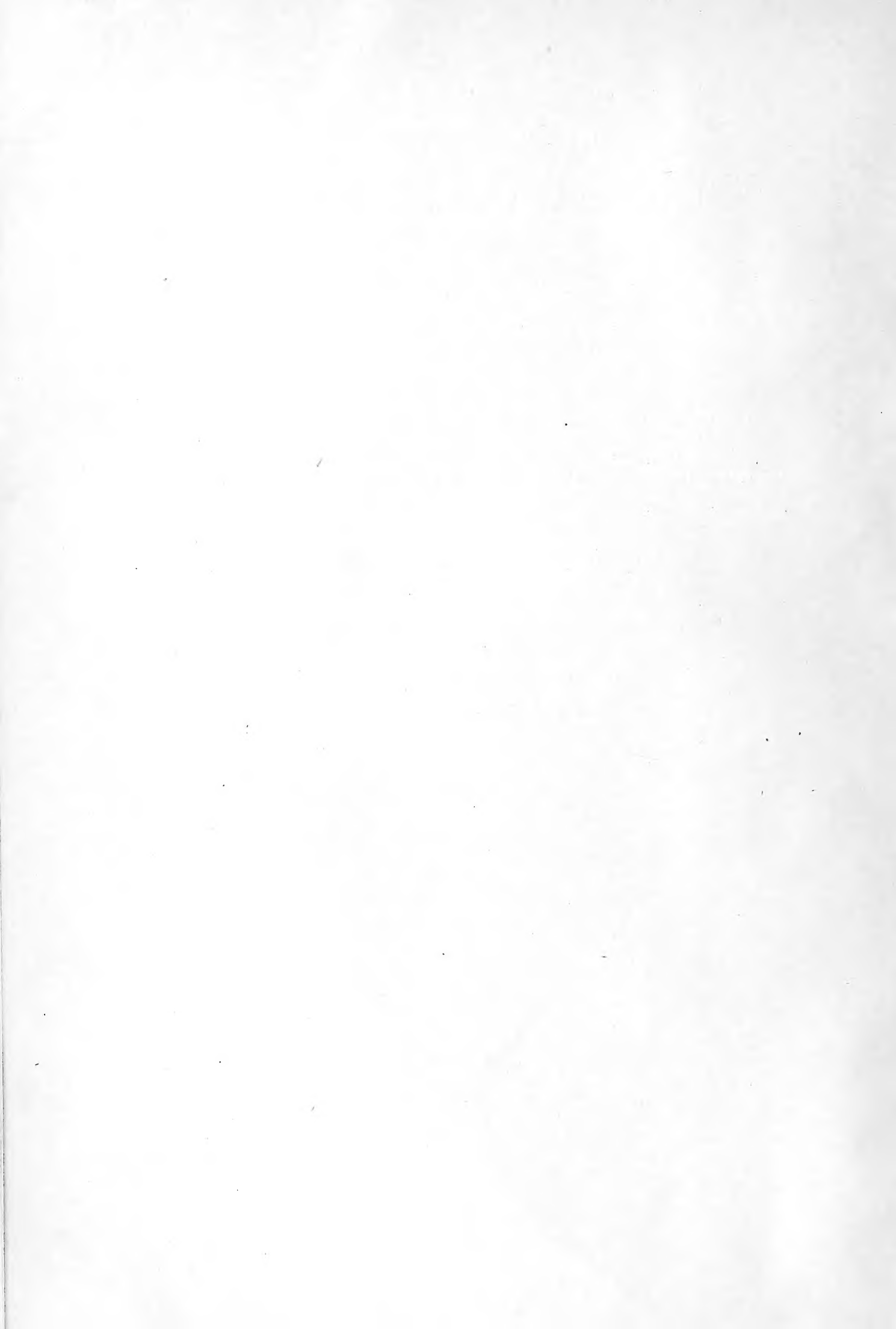
1911

WITH 21 PLATES, 5 FIGURES, 15 CHARTS, 3 DIAGRAMS, AND 2 MAPS.



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VOL. VI

FEBRUARY, 1911

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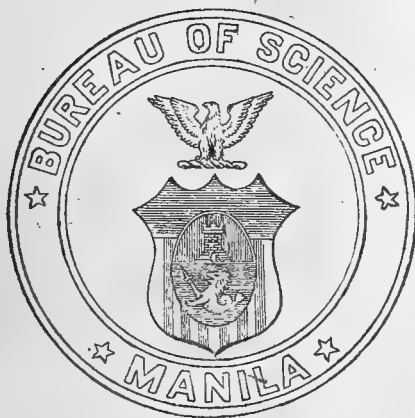
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# THE PHILIPPINE JOURNAL OF SCIENCE

## B. MEDICAL SCIENCES

VOL. VI

FEBRUARY, 1911

No. 1

### NUTRITION AND GROWTH: I.

By HANS ARON.

*(From the Physiological Laboratory, Philippine Medical School, Manila, P. I.)*

#### CONTENTS.

INTRODUCTION. Present knowledge of the relation between growth and nutrition.

The problem.

DESCRIPTION OF EXPERIMENTS. Methods, especially those used in the chemical analysis of the animals. Four sets of experiments on 14 dogs.

DISCUSSION OF EXPERIMENTS.

Influence of a restricted diet on growing dogs.

Effect on the weight and appearance of the animals.

Relative amount of change in certain parts of the body as compared with other parts.

Changes in the chemical constitution of the body.

Energy requirement and food consumption.

Biological considerations concerning the suppression of growth by restricting the food.

Energy required during growth.

The increase in weight as an index to growth, with special reference to children.

CONCLUSIONS.

#### INTRODUCTION.

As all the newly formed materials of the body are derived from the ingested food, nutrition must be one of the most important factors influencing the process of growth. Therefore, it is obvious that an intimate study of the relationship between nourishment and growth will furnish a valuable addition to our general knowledge of the physiology of growth.

The question of the influence of food on the process of growth is by no means merely theoretical. It has an important bearing on practical problems also, for the study of nutrition in modern pediatrics is gaining steadily in importance and much evidence has been accumulated showing how closely food and development are related. Only a thorough knowledge of the physiologic conditions of the process of growth and of its relation to nutrition can furnish a scientific basis for the feeding of infants as well as a clear insight into the problems involved.

Rubner,<sup>1</sup> during the past two years, has published extensive studies concerning the relationship of growth and nutrition. I have followed his ideas as closely as possible in my introductory discussion and I shall use his terminology, or the English equivalents, in preference to that which I employed in a paper<sup>2</sup> on the same subject written before his publication appeared. It is not my intention to discuss Rubner's fundamental work; nor his demonstration that the problem of the duration of life is involved in that of the number of calories metabolized during life. His theory that man, in contrast to all other mammals, occupies a particular position probably will not hold against the objections made by other authors.<sup>3</sup> However, Rubner's treatment of the fundamental questions concerning the application of the laws of energy to the problem of growth furnishes the basis for all considerations and investigations of this subject.

The original cause of the process of growth is the "capability of growing," as I have called it, or, better, the "tendency to grow," the term used by Rubner. While we are fairly well informed concerning the morphology of this process, its biology is dark. The "tendency to grow" results from the tendency of the juvenile cells or the cells in the juvenile organism to divide and to multiply. This tendency is strongest in the very young animal; it gradually becomes less marked, and finally is lost when the organism has grown enough; i. e., has passed the period of youth and become an adult. An adult organism under certain conditions may increase in certain parts of the body, but these processes known as "hypertrophy" (called forth by an increased demand of work on the muscles, heart, kidneys, etc.) or "pathologic growth" (tumor) are markedly different from that which we term "growth" in the sense of development.

The "tendency to grow" has an upper limit. This means that more than a certain quantity of new tissue can not be produced under any circumstances. This upper limit is variable, not only for the same individual according to the stage of development or age, but also in

<sup>1</sup> *Arch. Hyg.* (1908), **66**, 1-208; *Kraft und Stoff im Haushalte der Natur*, Leipzig (1909), 116-17.

<sup>2</sup> *Biochem. Ztschr.* (1908), **12**, 28-77.

<sup>3</sup> Hans Friedenthal, *Verhandl. d. physiol. Gesellschaft*, Berlin (1909), 93, and (1910), 22.

different individuals of the same species and especially in different species of animals. The rabbit and the dog have an upper limit which is very high, that is, these animals have a great "tendency to grow," while the human has only a small one.

The process of growth depends, not only upon this "tendency to grow," but also on the food. The "tendency to grow" induces the normal production of new tissues only when the material necessary for the construction of these new tissues is furnished by the food. The quantity of growth, to the upper limit of this tendency, is determined by the food. Rubner expresses the same idea when he says that "nutrition has a moderating influence on the process of growth." Therefore, the rate of growth depends upon two factors, the "tendency to grow" and the nutriment. Rapid growth takes place if this tendency is high in the cells and a sufficient quantity of food is taken to furnish all the substances needed. If there is no such tendency, then even the maximum intake of food will not lead to growth. It would naturally be expected that the converse should also be true; in spite of a high "tendency to grow" no growth should take place if the substances needed for this growth are not present in the food.

We must apply the laws of energy in studying the influence of nourishment on growth. From this point of view a growing animal requires food for two purposes: first, like the adult, to replace the energy expended in the production of heat and the work of the vegetative organs; and, second, for the formation of new body substances. This division of the needs of a growing animal into (1) energy required for maintenance and (2) energy required for growth, seems to be logical and it is adopted by the most competent authors dealing with this subject.<sup>4</sup>

The intake of energy, in order to enable an organism to grow, must exceed the requirement for maintenance, and this excess of energy is used for the formation of new body substances. However, in this instance it is not simply a question of energy in the form of calories; the protein intake also must exceed the demand for wear and tear and the excess of protein is stored in the form of new body cells. Similar considerations apply to certain inorganic constituents of food. Since the excess over the requirement for maintenance alone will be used in the formation of new body substances, the amount of growth will depend on the amount of this excess.

A further deduction leads to the conclusion that no growth will take place if there is in the food no excess over the amount of energy required for maintenance. In other words, it should be possible, by a proper restriction of the food, to suppress all growth. This conclusion has been accepted frequently without question. Gerhartz,<sup>5</sup> for example, regarded

<sup>4</sup> *Ostertag und Zuntz, Landwirtsch. Jahrb.* (1908), 37, 211.

<sup>5</sup> *Biochem. Ztschr.* (1908), 12, 97-118.

the requirement for maintenance of young dogs as equal to the caloric intake during periods in which the weight of these dogs neither increased nor decreased.

Will growth, suppressed by the necessary restriction in diet, cease entirely for an indefinite length of time? What becomes of an animal, suffering such a suspension of growth, when it is given an abundant food supply?

Rubner<sup>6</sup> states as follows in regard to these questions:

If the cells of a young animal are insufficiently nourished, the growth does not proceed. There is also no decrease of the energy metabolism (under which circumstances a decrease of the body temperature could not be avoided), but growth stops, without there being a loss of the "tendency to grow" in the near future. He bases this idea on experiments performed by O. Kellner with the silkworm and upon the work of Quetelet, who found the individuals of the working class to be smaller in stature than those of the better classes.

I shall here quote from the investigation of Kellogg and Bell<sup>7</sup> on the influence of diminished nourishment on silkworms (*Bombyx mori*).

These authors state that "there exists a very definite and constant relation between amount of food and size as indicated by weight, the starveling individuals being consistently smaller than the well-nourished, the lingering effects of this dwarfing being handed down even unto the third generation, although the progeny of the famine generation be fed the optimum amount of food. In case the diminished nourishment is imposed upon three or even two successive generations there is produced a diminutive, but still fertile, race of Lilliputian silkworms whose moths, as regards wing expanse, might join the ranks of the micro-Lepidoptera almost unremarked.

"An abnormal extension of the time needed for the metamorphosis follows upon a reduction of the food supply."

After my experiments were nearly finished and reported in part at the Far Eastern Association for Tropical Medicine in March,<sup>8</sup> 1910, there came to my attention, through the courtesy of Geheimrat Zuntz, a paper by H. F. Waters,<sup>9</sup> which deals with a problem similar to mine, but considered principally from the standpoint of animal husbandry.

This author reports on experiments on cattle which were fed with widely different quantities of food, in order to cause in some a normal gain in live weight (full fed); in others a fair growth but without allowing fat to be stored up (moderately fed); in still others only a slight gain in live weight (retarded development). In another group the feeding was so conducted as to allow of no increase in live weight (maintenance), and in a last group the animals were fed so as to lose in live weight (submaintenance). Waters has carefully studied the build of these animals, their size, and the size of their different parts. His results will be discussed in detail later in connection with my own.

<sup>6</sup> *Arch. Hyg.* (1908), **66**, 1-208; *Kraft und Stoff im Haushalte der Natur*, Leipzig (1909), 116-117.

<sup>7</sup> *Science*, (1903), **18**, 744, 746.

<sup>8</sup> *Berl. klin. Wchnschr.* (1910), 993.

<sup>9</sup> The influence of nutrition upon the animal form. XXX. Meeting of Society for the Promotion of Agricultural Science.

In view of the preceding considerations, it seemed quite interesting and promising thoroughly to study the influence of variations in the quantity of food, and more especially of a restricted diet, on the growth and development of mammals.

To solve this problem, we must first study the conditions surrounding the suppression of growth when the animal is at a standstill, receiving only the amount of food required for existence without growth. We must further endeavor to determine the maximum quantity of food which can be given without causing growth, and in what way varying additional amounts of food are used in the formation of new body substances.

A number of questions at once arise. Can we, by the restriction of food, suppress the process of growth entirely and, if so, for how long? If we suppress the growth, does the animal lose its "tendency to grow" as it ages? Does the capability for growing depend on the age, or on the size and weight of the animal? Is the growth of all parts of the body suppressed to the same degree, or is the "tendency to grow" of the various parts or organs of the body different? Do some parts develop or grow at the expense of the rest? It is known that in a starving animal the most important parts of the body, such as the heart and brain, suffer relatively much less loss in weight than do those of minor vital importance, namely, fat, muscles, and digestive glands. If different parts of the body do have a marked difference in the "tendency to grow," we shall be able to recognize this difference by suppressing the growth for a time.

The simplest and most usual method of estimating growth is by controlling the live weight. A constant increase in weight is conclusive evidence of the normal growth of a young animal. Some other indications of growth are increase in length and in other dimensions and certain changes which relate to the stage of development.

If the body weight remains constant, does this fact indicate that no growth is taking place? Growth, as we understand it from a biologic standpoint and in its relation to energy, constitutes a general, more or less equal, increase of all parts of the body. No growth means no change whatsoever in the body.

However, the live weight of an animal may not change at all, while internal relative "changes between the different parts of the body," of which I have already spoken, may take place. Obviously a constant live weight is not an indication of lack of growth in our sense. The question as to how far increase or constancy of live weight runs parallel with growth or cessation of growth is important and of practical value and deserves close attention. On the basis of these considerations the experiments to be undertaken may be outlined as follows.

A number of comparable animals must serve for each series of experiments, one of them receiving just enough food to keep its body weight

constant, the others, varying additional amounts so that a more or less intensive growth results. The work must include a careful control of the intake of food, of the body weight, and of the growth. Several difficulties are encountered in determining the latter. It is obvious that metabolism experiments are not suitable for this purpose, even if the respiratory metabolism be included. Such experiments, if extended over a long period, might reveal the total loss or gain of the body in certain substances, but would give no information concerning the behavior of the different parts and organs. What we really wish to know is the composition of the body at the beginning and at the end of the experiment.

A detailed analysis of the body appeals to me as the best method of gaining this information. Of course, we can not analyze the same animal twice. We can only determine its composition at the end of the experiment, and in order to secure data concerning the probable composition at the beginning we can either analyze a comparable control animal or find the composition by calculation from data obtained on other normal animals.

My experiments have been confined to dogs. A medium-sized dog is easy to handle, but large enough to permit a careful study and analysis of the different parts and organs of the body with a fair degree of accuracy.

#### DESCRIPTION OF EXPERIMENTS.

The general methods adopted were the following:

The animals were placed in a quarantine stable for from one to four weeks and the intestinal parasites, with which practically every dog in the Philippine Islands is infested, removed.<sup>10</sup> To this end, I gave from 0.5 to 1 gram of thymol by mouth daily for a period of from seven to ten days. Following this the dogs were allowed to become accustomed to their food and were all brought into a similar condition as to nutrition.

After this preparatory treatment, the animals were transferred to the experimental stable. This was a large, airy room constructed under an old wooden building with a wire fence on one side.<sup>11</sup> Four to six animals had at least 20 square meters of space and were fairly well protected from the sun and rain. Once or twice in the typhoon season they experienced a good drenching. The floor of the stable was nearly 2 meters above the ground and was constructed of small parallel boards with intervening spaces of about 1 centimeter to allow water to flow away easily. The room was cleaned every morning by flooding and once or twice each week it was disinfected with carbolic acid.

<sup>10</sup> It has not been proved that parasites influence the metabolism in a marked degree, but in other experiments dogs on a low diet became emaciated and died and their intestines contained numerous ascarides and tæniæ. I am inclined to believe that weak, poorly nourished animals suffer from these parasites.

<sup>11</sup> Only two dogs (A and B) which were kept considerably longer, since September, 1910, were placed in large metabolism cages in the animal house of the new laboratory building.

The food was prepared fresh every day, or every second day. The foods used were rice, canned condensed milk, sugar, and, later, commercial corn starch and meat. The meat was obtained fresh from cold storage; the fat was cut away and the rest passed through a grinder. Each food material was weighed and boiled with water in a weighed pot after adding sodium chloride or other salt mixtures. After cooling, water was added to a certain weight, the mixture stirred carefully, and the portion for each animal weighed. At the same time 50 or 100 grams of the mixture were placed in a large, well-closed jar with formalin until food specimens for twenty-five or fifty consecutive days were collected. These mixtures were used for analysis. Only meat and starch were fed to the animals during the greater part of the experiments.

The mixture at the beginning consisted of 1 part of starch and 10 parts of meat; later of 1 part of starch and 2.5 parts of meat. One hundred grams of food therefore consisted of 40 grams of meat; 16 grams of starch; and 44 grams of water and salts.

The animals were fed every forenoon between 9 and 10 o'clock. Each dog was transferred to a small cage and kept there until it had finished eating. During the first few weeks, it was necessary to give the food in two portions. After that period every dog ate his entire amount in from five to ten minutes.

The animals were weighed every one or two days before being fed, in order to have an exact control of their body weights as an indication of growth or of cessation of growth. The weights are recorded at intervals of five days so as not to make the tables too cumbersome. I have also prepared charts showing the weight of the animals and the amount of food administered at successive intervals.

At the conclusion of an experiment the entire animal was analyzed. The main object was to determine the weight and composition of the different parts of the body; particularly the percentage of the important constituents such as water, protein, and fat.

Dissection had to be done very quickly in order to avoid the rapid decomposition due to this climate. After the weight of the fresh material had been determined formalin was added. Formalin, while rendering work with the material rather disagreeable, nevertheless served admirably as a preservative and in no way affected the accuracy of the results of the analyses. It is a safe disinfectant, does not contain inorganic constituents, and can be removed readily by evaporation.

As a rule, it is very difficult to grind elastic or connective tissue in mills or grinders, even if the tissue is well dried. After being in contact with formalin it becomes hard and brittle. The formalin method effects the same result, therefore, as the more complicated one of freezing the tissues and passing them through a special grinder. By using formalin it is easy in a few hours to grind thoroughly in a small meat grinder the entire body of a dog weighing 5,000 grams.

In the first experiment the animals were killed with ether, but in the later ones by cutting the large blood vessels of the neck, the blood being collected in a weighed porcelain dish; then the body was placed in a large tared dish and the weight noted. The abdomen was opened and the gastro-intestinal tract ligated at the cardia and the rectum, and removed; the weight of the whole tract with the contents intact was taken. Following this the stomach and intestines were opened, the contents removed, and the gastro-intestinal tract cleaned and weighed again. Now organ after organ was separated, weighed (the necessary cross-sections being made to exclude gross pathologic changes), and placed with the others in a weighed, salt-mouthed bottle which was closed air-tight by means of a sheet of rubber and a wire fastener. Then from 40 to 50 cubic centimeters of

40 per cent formaldehyde were added, the bottle closed and weighed again. In the first experiment, the water content of each organ was determined.

The blood from the large vessels, the heart, lungs, and other organs was collected in a dish, which was weighed at the end of the experiment, after a known amount of formalin had been added. A part of this blood-formalin mixture was preserved in an air-tight bottle.

The skin was carefully removed, all subcutaneous fat being left behind. As yet no detailed analyses of the skin have been made.

The brain was removed, weighed, and kept with formalin in the manner just described.

A more exact analysis of the bones seemed advisable in the course of the later experiments, and a number of bones were carefully freed of all flesh and other adhering parts. This waste material was carefully collected. The cleaned bones were weighed and again preserved with formalin in a closed bottle.

At this time about three hours may have elapsed since the death of the animal. The remainder of the body, without skin, blood, organs, brain, and perhaps certain bones, was weighed again and then cooked with a fair amount of water in a large, weighed pot for from one to two hours. Following this operation the meat and bones were separated with forceps and knife, the juice being left with the meat. This separation generally required about half a day. Formalin was then added to bones and meat. The weighings were accurate to 1 gram. The bones were weighed on a large analytical balance, accurate to 0.1 gram.

In experimenting with a trial animal, I added formalin before separating bones and meat, but this procedure is not to be recommended, as the tissues around the bones become so hardened that it is almost impossible to remove them.

The bones preserved with formalin were dried on a hot day by exposure to the sun on a large plate from morning to afternoon and the weight of the air-dried bones was determined.

The meat, juice, and formalin were evaporated to the consistency of porridge, the total weight was determined, and the mixture placed in air-tight bottles.

Both bones and meat, after they have been treated with formalin, retain so much of this preservative that they are protected against decomposition. The entire animal, after all the above processes have been accomplished, is well preserved and contained in eight or ten handy bottles, so that it may be analyzed at leisure.

The organs and the meat of the body are passed several times through a sausage-meat grinder before analysis. Care must be taken not to lose any of the fluid; but even if there is much of this before grinding, it is completely absorbed afterwards. No appreciable loss occurs if the grinding is done quickly and the grinder then carefully cleaned. Several times I weighed organs before and after grinding and found a loss of only 3 to 4 grams per kilo, which is of no importance. Moreover, in our calculations, we assume that the total amount of organs, meat, brain, etc., is the weight of those materials before being subjected to the grinding process. We know the weight of the fresh organs. The formalin added being absolutely volatile, we can determine solids, as well as fat, protein, ash, etc., in the preserved materials and from these data we can calculate the composition of the original, fresh substance.

A difficulty in determining the weight of the entire skeleton arose from the fact that the bones were divided into two parts, one cooked, the other uncooked. It is not necessary to do this, but it seemed advisable in some instances. Only such bones as occur in pairs in the body had been removed and analyzed sepa-



rately before the rest were cooked. Hence it was only necessary to weigh the cooked bones which corresponded to those previously set aside and add this weight to the total in order to obtain the weight of the entire cooked skeleton. A slight error is involved in this process because the extract of the cooked bones is left with the meat. Another difficulty arises in the attempt to calculate the water content of the fresh meat and the fresh skeleton. We know the total solids in the skeleton and in the meat of the body; in the fresh stage we know only their weight taken together. I have assumed the percentage water-content of the freshly separated bones to be the same as that of the entire skeletal system. These values are sufficiently correct to give a clear picture of the differences in the relative proportions. I did not endeavor in these experiments to determine the composition of the whole body, but tried simply to illustrate the most striking differences.

In the determination of total solids, ash, and nitrogen (Kjeldahl) the usual methods were employed; in that of fat I used the method described of Baur & Barschall.<sup>12</sup> This procedure, which consists in the destruction of the nonfatty material by sulphuric acid and the extraction of the fat by shaking the solution so obtained two or three times with ether, is short and simple and gives as satisfactory results as the Soxhlet method. It is especially applicable in the Tropics, because during the greater part of the year the tap-water is so warm that it becomes necessary to use ice-water in the condensers to avoid losing too much ether.

*Experiment No. 1.*—Four dogs of one litter were used in experiment one. These were about two months old and all very much alike in appearance. In the beginning I had intended to study the influence both of different quantities and of different kinds of food upon growth and so gave meat only to two animals, and carbohydrates as well as meat to the other two.

Two of the four dogs were fed so that their weight increased rapidly (I and IV, Table 14), two were poorly nourished (II and III, Table 14). This experiment did not progress smoothly. The composition of the food was changed several times. From the sixteenth to the twentieth day, animals I, II, and III suffered from diarrhœa from some unknown cause. From this period until the fifty-sixth day no accident occurred. On the fifty-sixth day the native laboratory servant, who had been instructed to clean the stable with dilute carbolic acid solution, sprinkled pure phenol not only on the floor, but also on the dogs, and burned numbers I, II, and III so severely that they were promptly killed with ether to end their suffering. Number I escaped with only slight injuries. He was kept until the 8th of April, when he developed cramps and died in a few hours, apparently from internal injuries received from a fall.

During the relatively short period of this experiment animals I and IV increased in weight from about 1,400 to more than 3,000 grams.

<sup>12</sup> *Arch. a. d. kais. Gesndhtsmte.* (1909), 30, 55-62.

It is worth mentioning that number IV, receiving about 10 per cent less in calories than number I, very soon dropped somewhat behind the latter in weight.

EXPERIMENT I.—*Dogs I to IV.*

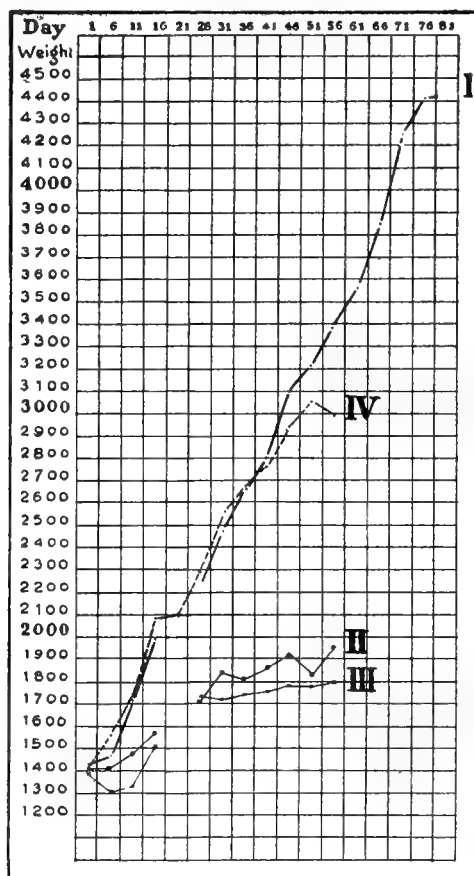


CHART 1.—Variations in weights of dogs I to IV of Experiment I.

Dogs II and III, which received practically the same amount of calories, increased but slightly in weight during the first forty days (from about 1,400 to 1,900 grams). The constancy in weight desired was reached between the fortieth and fiftieth day.

During the period of the experiment the appearance of the four animals changed considerably. While numbers I and IV were apparently well nourished and well proportioned, numbers II and III, although increasing in weight, began to appear emaciated. Their legs seemed to be unusually long and slender, while their heads appeared to be a trifle large in proportion to their bodies. I took a few measurements, which may illustrate this condition.

Dimensions of dogs on the fiftieth day of Experiment I.

No.	Entire length.	Circumference of chest.	Length of fore leg.	Length of hind leg.	Circumference of head.
	Cm.	Cm.	Cm.	Cm.	Cm.
II.....	45.0	30.0	25.6	31.2	20.5
III.....	43.5	27.5	24.8	30.3	20.3
I.....	51.0	33.0	28.0	33.0	20.6
IV.....	52.3	35.0	29.0	(?)	21.0

The term "live weight" in this paper is used to designate the weight of the entire animal before death. Those parts of the animal left after removing skin, internal organs, the digestive tract, and blood when it is bled to death, are called the "body." The "body" therefore consists of muscles, skeleton, nervous system, etc.

Analyses of the four animals used in Experiment I gave the following results:

TABLE 1, EXPERIMENT I.—Composition of dogs I to IV.

	Dog number—			
	II.	III.	IV.	I.
	Grams.	Grams.	Grams.	Grams.
Live weight.....	1,942	1,747	2,850	4,600
Body (muscles, skeleton, etc.).....	1,206	1,133	1,986	3,040
	Per ct.	Per ct.	Per ct.	Per ct.
Per cent of live weight.....	62.1	64.8	69.7	66.1

TABLE 2, EXPERIMENT I.—Weight of skin and organs of dogs II to IV.

	Fresh.			Dry.		
	Dog II.	Dog III.	Dog IV.	Dog II.	Dog III.	Dog IV.
	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.
Skin.....	282.6	238	333	104	89	120
Brain.....	60.30	57.10	59.86	10.62	10.67	11.12
Liver.....	95.25	85.55	140.07	22.09	21.30	35.33
Lungs.....	42.26	41.20	67.25	7.56	7.36	10.79
Heart.....	20.20	17.83	24.39	3.73	4.04	5.41
Kidneys and spleen.....	36.20	32.40	45.37	6.30	6.10	9.83
Internal organs, total.....	193.91	176.98	277.08	39.68	38.83	61.46
	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.
Per cent of live weight ..	10.00	10.10	9.70	2.04	2.22	2.15

TABLE 3, EXPERIMENT I.—*Weight of skin in per cent of live weight of dogs II to IV.*

Dog number—	Fresh.	Dry.
II.....	<i>Per cent.</i> 13.6	<i>Per cent.</i> 5.35
III.....	14.6	5.09
IV.....	12.0	4.21

TABLE 4, EXPERIMENT I.—*Composition of bodies of dogs I to IV.*

	Dog number—					
	II.			III.		
	Weight.	Per cent of—		Weight.	Per cent of—	
		Body weight.	Live weight.		Body weight.	Live weight.
	<i>Grams.</i>			<i>Grams.</i>		
Fat.....	30.7	2.5	1.6	21.8	1.9	1.3
Protein of muscles ..	167.0	13.9	8.6	168.0	14.9	9.6
Protein of bones.....	47.8	3.9	2.46	42.2	3.7	2.42
Ash of bones .....	68.3	5.7	3.52	61.5	5.4	3.52
Rest=(water, ash of muscles, etc.) .....	882.2	74.0	45.4	839.5	74.1	48.1

	Dog number—					
	IV.			I.		
	Weight.	Per cent of—		Weight.	Per cent of—	
		Body weight.	Live weight.		Body weight.	Live weight.
	<i>Grams.</i>			<i>Grams.</i>		
Fat.....	107.8	5.4	3.8	309.9	10.2	6.7
Protein of muscles ..	289.0	14.5	10.2	382.5	12.6	8.0
Protein of bones.....	49.5	2.5	1.74	105.5	3.5	2.29
Ash of bones .....	64.9	3.3	2.28	96.4	3.2	2.10
Rest=(water, ash of muscles, etc.) .....	1,474.7	74.3	51.7	2,145.7	70.5	46.7

*Experiment No. II.*—Two dogs of strikingly similar appearance from the same litter were used for the second experiment, which began on January 21, 1909. Number V weighed 2,200 grams; VI, 2,750 grams. The mother of the dogs was a large animal. Both animals passed through a preparatory period of three weeks during which, by giving different quantities of food, they were brought to nearly the same weight.

*Changes in weights of dogs V and VI (preparatory period).*

Date.	Dog V.	Dog VI.
	Grams.	Grams.
January 21 .....	2,200	2,750
February 1 .....	2,600	2,800
February 10 .....	3,100	3,200
February 18 .....	3,300	3,250

Number V, of smaller weight in the beginning, was selected to be so fed as to permit a normal growth; number VI, the heavier animal, was to be kept at a constant weight.

Only one accident occurred during the entire course of the experiment. (Table 15.) From the fourteenth to eighteenth day, number V suffered from overfeeding. By a slight restriction of food for two days, the trouble was remedied, but no increase in weight occurred from the eleventh to twenty-first day.

EXPERIMENT II.—Dogs V and VI.

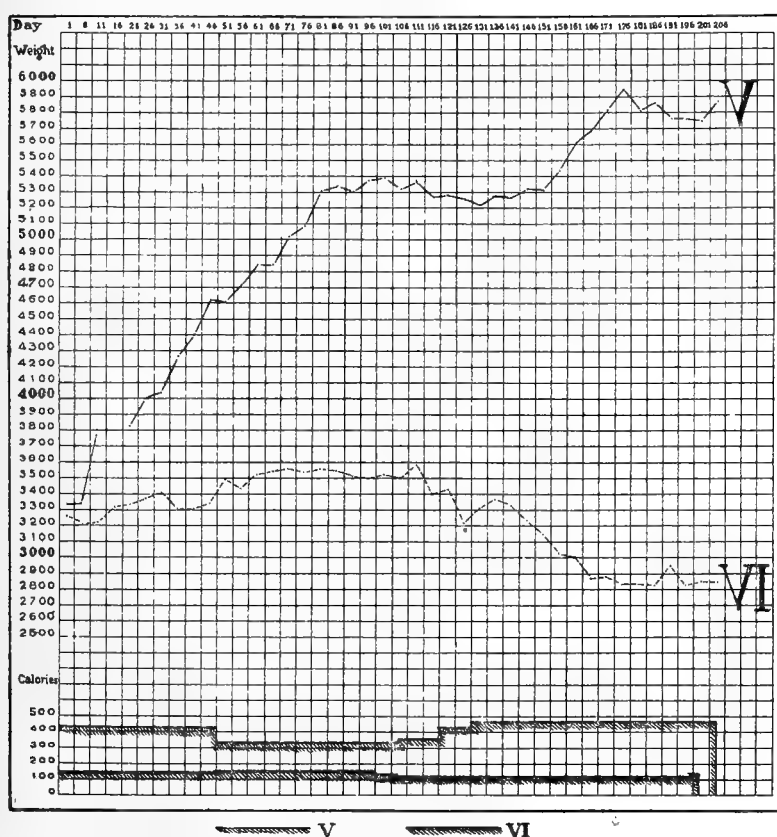


CHART 2.—Variations in weights of and amounts of food taken by dogs V and VI of Experiment II.

Number V, in the first fifty days, was given three times as much food as number VI, the latter receiving 140 calories only (meat 10 parts and starch 1 part). The body weight of number VI increased about 200 grams, while number V gained 1,300 grams. In the next fifty days, number V was given only 335 calories and the increase in weight was 750 grams. Number VI received a very slight increase (150 calories) because of its greater body weight, and gained about 100 grams.

The composition of the food was now changed, a mixture of 1 part of starch and 2.5 parts meat being supplied. The proportion of protein in the food seemed to me sufficient, about one-third of the total caloric intake being furnished by protein. Number V, when receiving as much as 480 calories, increased only slightly in weight; the animal now had reached almost the stage of adult life, and the greater part of the increase in weight was due to storage of fat and not to growth. The intake of number VI was at first reduced to 135 calories. Owing to the fact that the animal's weight still seemed to increase, I further reduced the food to about 120 calories, which amount, I thought, would furnish sufficient energy to keep the body weight constant. However, on this diet the animal, instead of gaining weight, lost, especially toward the last.

The changes in appearance which the two dogs showed during the course of the experiment are of great interest. Number V increased in weight and size just as any other normal dog would and was a fine looking, well nourished animal. Number VI resembled dogs numbered II and III of the first experiment, but the changes from the normal were more pronounced. Although increasing slightly in weight, the animal from day to day became thinner, but taller and longer. We see here the paradox of an animal becoming emaciated while gaining in weight. In the end, number VI seemed to be only skin and bones. Nevertheless, the dog was quite lively, jumping around and performing a really astonishing amount of muscular work.

On the one hundred and seventy-fifth day of the experiment a photograph of both dogs (Plate I) was taken, showing their general appearance and relative size, the distance from the lens of the camera being the same for both. The most surprising fact is that number VI, while weighing only two-fifths as much as number V, seemed to be not very much smaller. Indeed, the animal had grown all the time so far as length of body and size of extremities were concerned.

The following measurements taken on the one hundred and eighty-third day show that there is only a slight difference in length between the two dogs, while the circumference of number VI is considerably less than that of number V.

*Measurements of dogs V and VI on the one hundred and eighty-third day.*

	Dog number	
	V.	VI.
	<i>Cm.</i>	<i>Cm.</i>
Nose to os occipitale .....	15.5	15.0
Nose to tip of tail .....	53.0	49.0
Length of fore leg .....	35.0	34.0
Length of hind leg .....	38.5	37.5
Circumference of head .....	26.5	25.5
Distance from ear to ear .....	8.4	7.5
Circumference of chest .....	37.5	30.0

From the one hundred and ninetieth to the one hundred and ninety-fifth day of the experiment, number VI no longer exhibited such liveliness and muscular strength, but appeared to be lazy and weak. Therefore, on the two hundredth day, it seemed necessary to increase the amount of his food. At first, 150 calories were given, but the animal was apparently already too weak to recover, for it died on the morning of the two hundred and third day, doubtless of general weakness. No sign of disease was shown at autopsy except extreme emaciation, an absolute lack of subcutaneous fat, general anæmia of all the organs, and an unusually soft consistency of the muscles.

Number V was killed as a control animal a few days later by bleeding. The animal showed a well-developed layer of subcutaneous and visceral fat and normal internal organs.

The analyses gave the following results.

TABLE 5, EXPERIMENT II.—*Composition of dogs V and VI.*

	Dog V (5,885 grams).		Dog VI (2,708 grams).	
	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.
	<i>Grams.</i>		<i>Grams.</i>	
Brain .....	<sup>a</sup> 52	0.90	<sup>b</sup> 58	2.00
Liver .....	153	2.60	97	3.62
Heart .....	39	0.66	17	0.61
Lungs .....	60	1.01	29	1.07
Spleen .....	12	0.21	2	0.01
Kidneys .....	35	0.60	22	0.81
Digestive tract empty .....	387	6.58	155	6.00
Other internal organs .....	236		52	
Body (muscles, bones, etc.) .....	3,835	65.2	1,624	60.0
Skin .....	662	11.2	339	12.5
Blood .....	<sup>c</sup> 346		<sup>d</sup> 40	
Content of stomach and intestines by difference .....	168		273	

<sup>a</sup> Dry 12.8 grams.

<sup>c</sup> Killed by bleeding.

<sup>b</sup> Dry 11.2 grams.

<sup>d</sup> Died; blood collected from large vessels after death.

TABLE 6, EXPERIMENT II.—*Weight of certain of the bones of dogs V and VI.*

	Dog V.		Dog VI.	
	Fresh.	Dry.	Fresh.	Dry.
	Grams.	Grams.	Grams.	Grams.
Femur.....	28.35	16.53	27.2	9.85
Tibia-fibulare.....	25.00	15.14	23.2	9.77
Scapula.....	13.55	6.68	11.4	5.05
Humerus.....	27.45	15.63	26.8	9.84
Radius.....	11.65	7.36	11.05	4.84
Ulna.....	10.30	6.54	10.9	4.85
3 ribs (5, 6, 7).....	10.70	5.02	8.75	3.48
Total.....	127.00	72.80	119.3	47.68
Per cent of live weight.....	Per cent.	Per cent.	Per cent.	Per cent.
	2.16	1.24	4.41	1.76

TABLE 7, EXPERIMENT II.—*Percentage composition of dogs V and VI.*

	Dog V.			Dog VI.		
	Weight.	Per cent of—		Weight.	Per cent of—	
		Body weight.	Live weight.		Body weight.	Live weight.
	Grams.			Grams.		
Fat.....	271.5	7.1	4.6	7.7	0.5	0.3
Protein of muscles ..	632.3	16.5	10.7	147.6	9.0	5.4
Protein of bones ....	138.6	3.6	2.4	110.1	6.8	4.0
Ash of bones .....	131.0	3.4	2.2	126.3	7.8	4.7
Remainder of body, (muscles, ash, etc.)	2,661.6	69.4	45.2	1,232.3	75.9	45.5
Fat in organs .....	137.7		2.3	5.0		0.2
Protein in organs ....	120.6		2.0	51.1		1.9
Total fat .....	409.2		6.9	12.7		0.5
Total protein.....	891.5		15.1	308.8		11.3

TABLE 8, EXPERIMENT II.—*Composition of bones of dogs V and VI.*

	In the fresh bones.		In the solids.	
	Dog V.	Dog VI.	Dog V.	Dog VI.
	Per cent.	Per cent.	Per cent.	Per cent.
Water.....	42.76	60.02		
Protein.....	22.06	18.05	38.54	45.15
Ash.....	20.79	20.70	36.32	51.78
Fat.....	12.34	0.09	21.55	0.23



TABLE 9, EXPERIMENT II.—Water and solids in different parts of the body.

	Dog V.		Dog VI.	
	Total solids.	Water.	Total solids.	Water.
	Per cent.	Per cent.	Per cent.	Per cent.
Blood.....	<sup>a</sup> 18.84	81.16	<sup>a</sup> 5.10	94.90
Brain.....	24.60	75.40	19.31	80.69
Bones.....	57.24	42.76	39.98	60.02
Muscles.....	29.12	61.88	15.24	84.76

<sup>a</sup> Protein =  $N \times 6\frac{1}{4}$ .

*Experiment No. III.*—For the third experiment seven dogs were taken originally. Number VIII matched number IX, and number X matched number XI extremely well, while numbers VII, XII, and XIV were comparable fairly well.

EXPERIMENT III.—Dogs VIII, XI, XII, XIV.

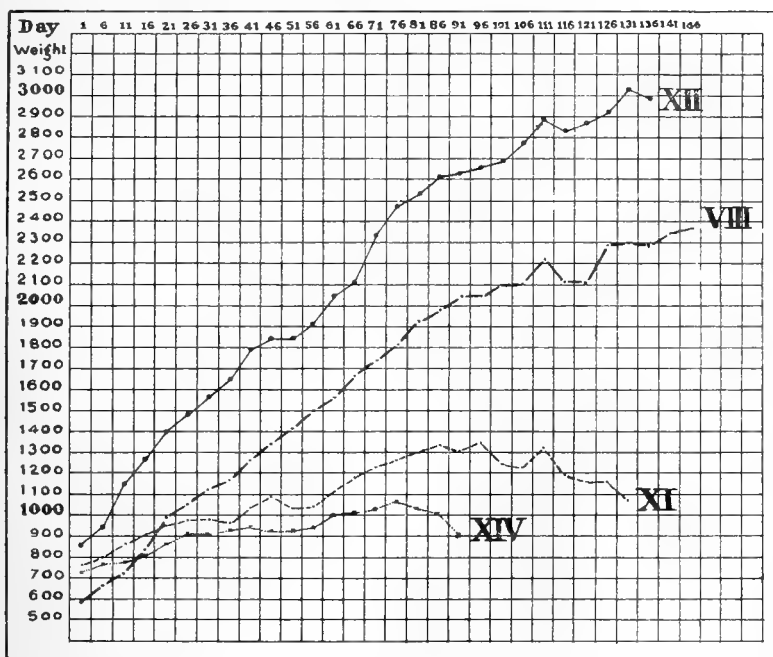


CHART 3.—Variations in weights of dogs VIII, XI, XII, and XIV of Experiment III.

Dogs numbers VII, IX, and X were killed on the eighteenth day of the experiment through the same accident by which animals I, II, and III were lost. Only four dogs were left, these being comparable more by reason of age and weight than by descent. In spite of the unfortunate accident, this experiment was continued for some time. (Table 16.) It was planned to keep the weights of dogs numbers XI and XIV constant. For twenty days each animal received 110 calories and their

weights increased from 760 to 950, and from 732 to 866 grams, respectively. Number XIV was given about 75 calories. On this diet its weight remained practically stationary. The animal became thinner and weaker from day to day and died from emaciation and weakness on the ninety-first day of the experiment. The body was not analyzed chemically because it was thought at the time that the composition of the starved animal would be of no special interest.

Number XI after the first twenty days received 90 calories, then 95, and finally 100 calories, and its body weight increased from about 950 to 1,150 grams. This dog presented the same picture as number VI of the first experiment, for it became thinner and taller during the entire period. It was killed on the one hundred and thirty-sixth day and analyzed. (Tables 10 and 11.)

Dog number VIII, the lightest at the beginning of the experiment, was given an ample supply of food and during one hundred and forty-five days increased from 600 to 2,350 grams. Dog number XII, weighing 850 grams at the beginning, received the equivalent of but a few more calories, but its weight nearly reached 3,000 grams in one hundred and forty days. Both animals were analyzed and a study of table number 11 reveals the interesting fact that dog number VIII had a much greater tendency to put on fat, while the muscles of number XIII increased markedly in weight. This is explained by the fact that number VIII was of a smaller breed than number XII.

TABLE 10, EXPERIMENT III.—*Composition of dogs VIII, XI, and XII.*

	Dog XI (1,100 grams live weight).		Dog VIII (2,375 grams live weight).		Dog XII (3,000 grams live weight).	
	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.
	<i>Grams.</i>		<i>Grams.</i>		<i>Grams.</i>	
Liver .....	48		88		78	
Heart .....	10		21		21	
Lungs .....	11		19		26	
Spleen .....	2		5		7	
Kidneys .....	24		27		24	
Digestive tract .....	102		159		223	
Remaining internal organs .....	45		89		85	
Total internal organs .....	242	22.0	408	17.2	465	15.5
Brain .....	49	4.5	48	2.0	57	2.9
Body .....	645	58.6	1,413	59.5	1,946	64.8
Skin .....	134	12.2	309	13.0	294	9.8
Blood .....	66	6.0	138	5.9	197	6.6
Content of stomach and intestines by difference .....	23		107		198	

TABLE 11.—*Fat and protein in organs and muscles of dogs VIII, XI, XII.*

	Dog VIII (2,375 grams live weight).		Dog XII (3,000 grams live weight).		Dog XI (1,100 grams live weight).	
	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.
	<i>Grams.</i>		<i>Grams.</i>		<i>Grams.</i>	
Fat in muscles -----	51.9	2.2	30.1	1.0	7.0	0.6
Fat in organs -----	21.6	0.9	19.9	0.7	4.3	0.4
Total fat -----	73.5	3.1	50.0	1.7	11.3	1.0
Protein in muscles --	155.9	6.6	229.4	7.6	54.0	4.9
Protein in organs ----	61.0	2.6	78.6	2.6	31.9	2.9
Total protein ----	216.9	9.2	308.0	10.2	86.1	7.8

*Experiment No. IV.*—Experiment number IV was the most successful one. Four dogs (A, B, C, D) of the same litter, about 5 weeks old, were treated with thymol early in July, 1909, and prepared for the experiment. The animals were as nearly alike as could be desired in size and general appearance. The experiment began August 1, 1909. On the fortieth day the four dogs were of nearly the same weight and were photographed. On the forty-fifth day, dog D was killed and analyzed for comparison. (See Table 13.) Dog B was allowed to grow as rapidly as possible; dog C was not given as abundant a supply of food as B, and dog A was fed only a sufficient amount to keep his body weight constant.

The mineral constituents of the food were disregarded in the experiments described above. If a young, rapidly growing dog is fed a diet of meat and starch such as was used in these experiments, it very probably will receive an insufficient supply of calcium salts. In order to remove this possible source of error there were added to the daily food of each dog from 1.0 to 1.5 grams of calcium phosphate in addition to the sodium chloride.

The experiment progressed smoothly so far as dogs A and B were concerned (see Table 17), but on the one hundred and twenty-second day dog C was taken ill suddenly and died in about twenty hours. The cause of death could not be determined at autopsy; it may have been distemper.

Dog B, which received from 400 to 680 calories daily, increased in weight from 1,500 grams (2,000 on the fortieth day) to about 7,400 grams on the five hundredth day.

Dog A was not kept on quite so low a diet as the other animals (VI, XI, and XIV), the body weights of which were to remain constant: at

first it received 110, then 130, and, finally, from the one hundredth day, 175 calories per day. Its body weight increased so little that it could be regarded as practically constant.

EXPERIMENT IV.—*Dogs A to D.*

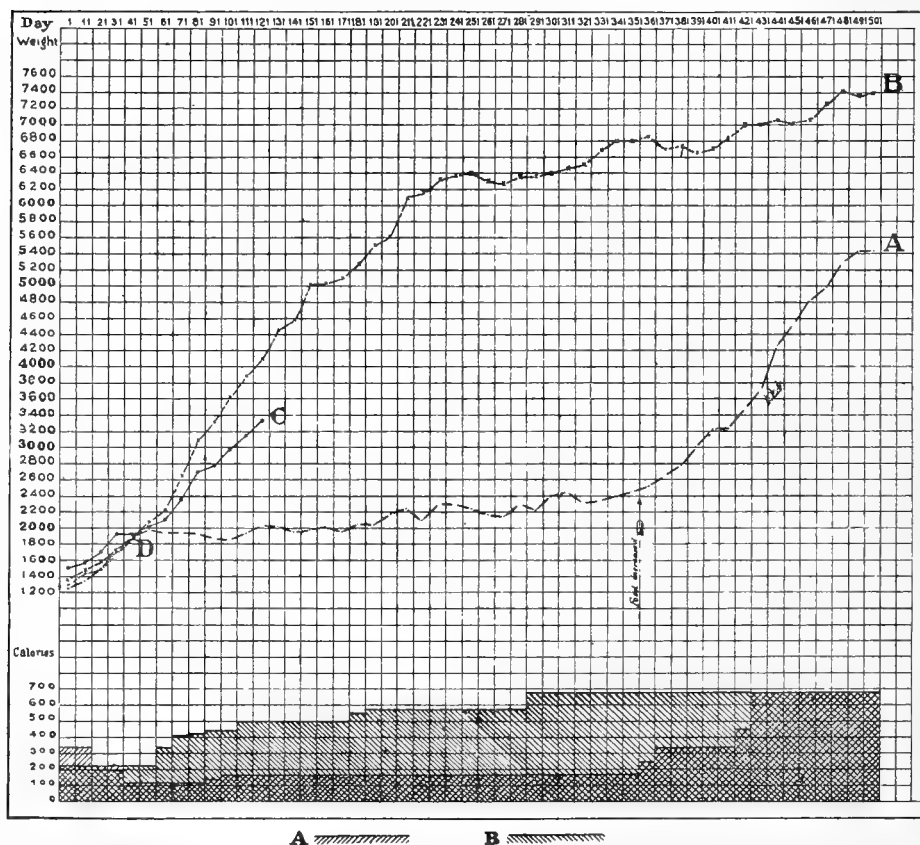


CHART 4.—Variations in weights of and amounts of food taken by dogs A to D of Experiment IV.

The animal in every respect presented the same type of development as number VI. It gradually became thinner, taller, and longer to the two hundredth day, when it no longer changed in appearance. The animal consisted mainly of skin and bones, but it still had enough muscle to enable it to move with vivacity, in fact it was more active than dog B, although the latter was three times as heavy. A photograph of both dogs was taken on February 15, the one hundred and ninety-ninth day. This, better than any description, shows the difference in size and appearance of the two animals. (See Plate II.)

The dogs were kept for about one hundred and fifty days longer. Dog A continued to receive the same diet. The diet of B was increased to 680 calories per day. The body weight of dog A remained practically constant and the dog did not change appreciably in general appearance.

Dog B, with a more than ample diet, became somewhat larger and much fatter, and increased in weight from about 5,500 to 7,000 grams.

The experiment was continued in this way to the three hundred and fiftieth day, when another photograph (Plate II) was taken. At the same time the animals were measured. (See Table 12.) On comparing the photographs of the dogs taken on the two hundredth and the three hundred and fiftieth day, it is apparent that during these last five months dog A had not only kept its body weight constant, but also had not grown.

Both animals were more than one and one-fourth years old at this time, and had reached the age at which dogs usually cease to grow. This is proved by the fact that dog B in spite of its ample diet showed no further increase in size and only very little in weight.

If the animals (A and B) had been killed at this time the increase or decrease in weight of the different organs and parts of the body since the forty-fifth day, as compared with the body of the control dog D, could have been determined exactly. We would then have had further evidence bearing upon the question as to which organs or parts of the body increase at the expense of others. However, I considered that I had already accumulated sufficient data on this point. These animals had now become invaluable for the solution of another and biological problem, namely, whether dog A, if it were now to be given an abundance of food, would increase in weight and size and make good the growth it lost in its youth. It also was necessary to determine whether dog A would finally attain the same weight and size as dog D.

Therefore, starting on the three hundred and fifty-fifth day, the food of number A was augmented to 230, 280, 340, 450, and finally 680 calories each day. An increase in body weight was noticed almost at once and the animal continued to gain steadily. At the same time it became rounder, the bones did not show through the skin as they did before, and the sharp angles disappeared. The diet from the four hundred and thirty-first day was the same as that of the control dog B, and following this a further increase in weight was observed. The animal continued to fatten, but apparently it did not increase in length nor in height. In order to determine if this dog still had the capacity for growing, to offset the lack of growth brought about by his restricted diet in youth, the same measurements were taken on the five hundredth as were recorded on the three hundred and fiftieth day, before the food was increased. These values are given in the following table and indicate clearly that during this period dog A, while receiving a more than ample diet and gaining in weight from 2,450 to 5,440 grams, practically did not increase in length or height, but only very greatly in circumference.

TABLE 12.—Weights and measurements of dogs A and B.

	Dog A.		Dog B.	
	355th day.	500th day.	355th day.	500th day.
Weight in grams .....	2,450	5,440	6,850	7,400
	<i>Cm.</i>	<i>Cm.</i>	<i>Cm.</i>	<i>Cm.</i>
Length from nose to atlas .....	16.0	16.0	18.0	18.2
Length from nose to os coccygis .....	54.0	55.5	66.0	66.0
Length from nose to end of tail .....	71.0	74.0	88.0	89.0
Distance from ear to ear .....	8.0	9.4	11.4	11.5
Circumference of head .....	23.5	26.5	28.5	29.0
Circumference of neck .....	15.5	23.0	27.0	28.0
Circumference of chest .....	28.0	39.5	43.0	47.0
Circumference of abdomen .....	21.0	34.0	33.0	37.0
Length of fore leg .....	25.0	26.0	34.0	34.5
Length of hind leg .....	31.0	31.0	37.5	37.5
Height from ground .....	29.5	31.5	35.5	36.0

On the five hundredth day, as compared with the three hundred and fiftieth, the aspect of dog A had changed entirely. The slender, emaciated animal had become an overfatted but dwarfed dog. Photographs of both A and B were taken on the five hundred and first day. (See Plates III and IV.) It is apparent that dog A, in spite of the ample diet given during the last five months, had lost the "tendency to grow." However, because of the ample food which had been given to it, it was able to store up fat, thus increasing in weight and thickness, but not in size.

It having been proved that dog A had lost its normal capability of growing, it was decided to finish the experiment by killing and analyzing both animals. This was done on the five hundred and fifth and five hundred and sixth day for A and B, respectively. The autopsies showed no remarkable features, except a great amount of fat in dog A, the subcutaneous layer as well as the muscular and mesenteric fat being considerably greater in amount than that of its normal brother B. The weights of the organs and the bones, selected as usual, were determined. (Table 13.)

TABLE 13, EXPERIMENT IV.—*Composition of dogs A to D.*

	Dog D (killed Sept. 18, 1909).	Dog C (died Dec. 3, 1909).	Dog A (killed Dec. 20, 1910).	Dog B (killed Dec. 21, 1910).
	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>
Live weight.....	1,985	3,410	5,474	7,178
Liver.....	62		152	171
Heart.....	13		38	59
Lungs.....	20		58	87
Spleen.....	5		12	17
Kidneys.....	18		32	59
Digestive tract empty.....	125		250	316
Remainder of internal organs.....	79		167	227
Total weight of organs.....	322		709	936
	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>
Organs in per cent of live weight.....	16.2		12.9	13.0
	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>
Blood collected.....	95		263	418
Skin.....	320	601	808	869
Brain.....	52	60	56	65
Remainder of body=(muscles, bones, etc.).....	1,164		3,637	4,816
	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>
Body in per cent of live weight.....	58.6		66.4	67.0
	<i>Grams.</i>		<i>Grams.</i>	<i>Grams.</i>
Content of intestines by difference.....	84		57	141
Weight of:	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>
Femur.....	11.0	17.3	16.23	24.74
Tibia-fibulare.....	8.6	15.1	12.89	20.63
Scapula.....	5.0	8.8	7.10	13.61
Humerus.....	10.0	16.85	15.45	22.84
Radius.....	4.05	7.75	5.92	9.16
Ulna.....	3.75	7.1	5.72	8.59
Three ribs (5, 6, 7).....	4.25	8.8	5.78	9.90
Total weight of nine bones.....	47.00	81.6	69.09	109.47
	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>
Total of nine bones in per cent of live weight.....	2.37	2.39	1.26	1.53

Both animals had been given an excess of food to enable them to grow to the greatest possible extent and therefore the relative amounts of fat and flesh, as compared with the skeletons, were larger than in the case of the control dogs C and D which had been killed more than a year before; the bones in both animals were relatively lighter. However, it will be seen that the bones of dog A, in which the growth was suppressed in the first period of the experiment, weighed considerably less in proportion to the total live weight than was the case with the normal control animal B, this being the result of the excessive feeding of A. Plate IV shows several bones of both A and B, and demonstrates that the various bones of A had not reached the dimensions of those of its normal brother, in spite of the fact that for five months it had been given a more than ample diet.

#### DISCUSSION OF EXPERIMENTS.

##### INFLUENCE OF A RESTRICTED DIET ON THE WEIGHT AND APPEARANCE OF GROWING DOGS.

In six animals (II, III, VI, XI, XIV, A) an attempt was made to suppress growth by restriction of food. All these animals were far behind their normal brothers (I, IV, V, VIII, XII; B and C, respectively) in weight. In spite of the restricted diet there was a slight increase in weight in the first group. The weight of dog number VI of the second set increased but very slightly in the first period, after that it remained constant, and decreased only at the end of the experiment. Number XI of the third set also lost but very little; the weight of number XIV remained practically constant. The weight of dog A of the fourth group remained nearly the same for ten months (fortieth to three hundred and fiftieth day), increasing but very slightly. The weight in all these dogs was so nearly constant that we are justified in so regarding it, the increase or decrease amounting to a few grams only. Did a cessation of growth take place with this constancy in weight? By no means! We have already seen that in spite of the constancy of weight all the dogs increased in length and height. At the same time the animals became leaner, fat and muscles diminished, the well-rounded form of the body disappeared, and the bones became visible in outline directly under the skin. The dogs when in this condition were by no means weak. They jumped about and were often more active than their normal brothers, but the latter had to carry nearly three times as much live weight.

This stage, in which the dogs grew leaner but longer and taller, while the weight was practically constant, lasted for from three to five months, varying somewhat with the degree of restriction of the food. If now the restricted diet was continued, when the animals were emaciated to an extreme degree, they died of inanition following a slight loss of



weight, but if the food was increased slightly, it was possible to keep the emaciated animal at a constant weight.

From the two hundredth until the three hundred and fiftieth day—that is, for five months—dog A was kept at a constant weight and there was no noticeable change in its size nor in its appearance; in fact this constancy indicated a cessation of growth. Therefore we must conclude that it is possible by a suitable restriction of diet to maintain young, growing dogs at a constant weight for considerable lengths of time. While the weight remains constant, important changes occur in the animal's body. These consist in a continuous increase in the length and height of the dog, combined with a more or less extreme emaciation.

Apparently, in spite of the constancy of weight, the skeleton grows and increases both in size and mass. If this be true, other parts of the body must have lost in mass. In all probability not only the relative masses of the different parts of the body, but also the quantities of the various body constituents, have changed considerably. Information concerning these alterations is furnished by the analyses of the bodies of the animals.

RELATIVE AMOUNT OF CHANGE IN CERTAIN PARTS OF THE BODY AS COMPARED  
WITH OTHER PARTS.

The skeletal system shows the most striking difference in general composition. The quantities of protein and ash in the bones of the three dogs, IV, II, and III, are nearly the same in spite of the differences in weight, number IV, 2,850 grams; number II, 1,940 grams; and number III, 1,750 grams. The weight of the bones (ash and protein) in relation to the live weight is considerably higher in dogs number II and III (9.6 per cent and 9.1 per cent) than in dog number IV<sup>13</sup> (5.8 per cent).

We find even more pronounced differences in comparing the compositions of dogs V and VI. Several corresponding bones of these two animals were isolated and analyzed. The weight of each bone of dog number VI was not much less than was the corresponding bone of dog number V, although the body weight of the former was 5,885 grams and of the latter 2,710 grams. The total weight of the nine bones selected from the normal dog, number V, was 127.0 grams or 2.16 per cent of the live weight; the bones from the dog of constant weight, number VI, weighed 119.4 grams or 4.41 per cent of the live weight.

In experiment IV, I isolated the corresponding bones from two other

<sup>13</sup> The bones of dog number IV contain proportionally more protein and less ash than those of numbers II and III. This fact is still more pronounced in dog number I. These animals were fed on a diet poor in calcium (meat and starch without addition of lime) and the changes in the skeletal system correspond to those described by me as occurring as a consequence of such a diet.

young dogs of the same litter, at a time when they were of different weights and different ages. These animals (C and D) were of equal weight at the time D was killed and analyzed. Dog C was then fed normally for about seventy-five days and analyzed. These results show:

*Live weight and weight of nine bones, dogs D, C, and V.*

Dog.	Live weight.	Weight of 9 corresponding bones.	Per cent of live weight.
	<i>Grams.</i>	<i>Grams.</i>	
D -----	1,985	47.0	2.37
C -----	3,410	81.6	2.39
V -----	5,885	127.0	2.16

The weights of the corresponding bones expressed as percentages of the respective live weights are nearly the same in dogs D, C, and V. We may assume that in dog VI, which was kept at constant weight, these bones amounted to about 2.2 per cent of its live weight before the experiment began. Hence, on or about the first day of the experiment, when the animal weighed 3,200 grams, these nine bones had a weight of about 70 grams. After about two hundred days, the same animal weighed 2,800 grams only, and the bones had increased in weight to 119 grams.

The composition of a normal dog is approximately constant (Voit,<sup>14</sup> Pfeiffer,<sup>15</sup> Stockhausen<sup>16</sup>), the skeleton 15 per cent, the muscles (flesh) 50 per cent of the live weight. The skeleton plus flesh of our normal dog V was found to equal 65.2 per cent of the live weight, which is in very close agreement with these figures. We are justified in regarding 15.0 per cent as skeleton, 50.2 per cent as flesh, 65.2 per cent skeleton and flesh.

The entire skeleton therefore would weigh 883 grams. Now, if we know that the same fraction of fresh bones, which in dog V weighed 127 grams, was 119.4 grams in dog VI, we can apply the results obtained with the nine bones to the entire skeleton, as follows:

$$\frac{883 \times 119.4}{127} = 830 \text{ grams.}$$

<sup>14</sup> *Ztschr. f. Biol.* (1894), **30**, 510-522.

<sup>15</sup> *Ibid.* (1887), **23**, 340-380.

<sup>16</sup> *Biochem. Ztschr.* (1909), **22**, 244.

In the beginning of the experiment the skeleton weighed 15 per cent of 3,200 grams = 480 grams. From this figure the following values are obtained for the increase of the skeleton:

	Live weight.	Skeleton.
	Grams.	Grams.
Beginning of experiment.....	3,200	480
End of experiment.....	2,800	818
Increase.....		338

Both these experiments (I and II) show conclusively that, *if a growing dog is kept at a constant weight, or even at a slightly decreasing weight, the bones continue to increase in weight and therefore to grow, although not quite so rapidly as in a normally fed control animal.* If the bones have absolutely and relatively increased in weight, while the total weight of the animal has been kept constant, it is obvious that other parts of the body must have lost in weight.

The organs are apparently not involved in this process of consumption. In the first experiment the weight of lungs, liver, heart, spleen, and kidneys only was taken; all these organs had their normal blood content, the animals not being killed by bleeding as was the case later. The total weight of these organs amounted to 10.0 per cent and 10.1 per cent, respectively, of the live weight of the two dogs which were on a low diet, as compared with 9.7 per cent in the normal one. In experiments II, III, and IV the weight of all the organs of the thorax and abdomen was determined, the intestinal tract having been cleaned previously. The results are summarized in the following table:

Number of dog.	Live weight.	Total weight of organs.	Per cent of live weight.
	Grams.	Grams.	
V (N) <sup>a</sup> .....	5,885	822	14.0
VI (C) <sup>a</sup> .....	2,710	374	13.7
XII (N) .....	3,000	465	15.5
VIII (N) .....	2,375	408	17.2
XI (C) .....	1,100	242	22.0
D (N) .....	1,985	322	16.3

<sup>a</sup> (N) The dog grew under normal conditions. (C) The dog was kept at a constant weight.

The values vary somewhat, but there is no indication that the organs of the animals kept on a lower diet lost in weight. On the contrary, the percentage weight of the organs of number XI is slightly higher than that of the control dogs of the same age, but of more or less normal live weight.

In experiment I the proportion of total solids in the organs was also determined. As Table 2 shows, there is practically no difference in the amount of dry organs, expressed in percentage of live weight, for the three different dogs.

There is little to be said about the behavior of the different organs. It appears in general that those of the digestive tract (liver, kidneys, and intestines) have increased somewhat, while the others, such as the spleen, heart, and lungs, have suffered a slight loss.

The brain deserves special consideration. In experiment I the weights of the brains of the three dogs did not differ in the same way as those of the other organs. Their weights were nearly identical, in spite of the difference in body weight of the animals. The same holds true for experiment III. In experiment II the dog of smaller body weight (VI) had a heavier brain than the normally developed animal (V). However, Table 9 shows that the absolute amount of solids in both brains is nearly the same, being slightly smaller in that of dog VI than in that of dog V.

*Live weight and brain weight in eight dogs.*

Number of dog.	Live weight.	Weight of brain.
	<i>Grams.</i>	<i>Grams.</i>
II (C) <sup>a</sup> .....	1,940	60.3
III (C).....	1,750	50.1
IV (N) <sup>a</sup> .....	2,850	59.9
V (N).....	5,885	52.0
VI (C).....	2,710	58.0
XI (C).....	1,100	49.0
XII (N).....	2,375	48.0
VIII (N).....	3,000	57.0

<sup>a</sup> (N) Grew under normal conditions. (C) Kept at a constant weight.

The figures in the foregoing table show conclusively that the brain has nearly the same weight in a dog kept at a constant weight as in a normally developed animal.

The weight of the brain in relation to the body weight in a younger animal is higher than in an older one, and the brain does not grow in the same proportion as do the other organs. This is well illustrated

by the following data, taken from those recorded for the two dogs of experiment IV, one of which (D) was killed seventy-five days before the other (C). While the live weight had increased from about 2,000 to 3,400 grams, the weights of the brains at the two different periods are 52 and 60 grams, respectively; i. e., there was 70 per cent increase in the live weight, and only 15 per cent increase in brain weight.

According to data taken from Monti<sup>17</sup> the brain of a child increases in weight from three to four times, while the weights of other organs increase about ten times.

The skin shows a slightly higher percentage of the body weight in those animals kept at a constant weight than in the normal, control dogs.

	Dog.	Weight of skin in per cent of body weight.	
		Fresh.	Dry.
Experiment I -----	II (C) <sup>a</sup> -----	13.6	5.35
	III (C) -----	14.6	5.09
	IV (N) <sup>a</sup> -----	12.0	4.21
Experiment II -----	V (N) -----	11.2	-----
	VI (C) -----	12.5	-----
Experiment III -----	XI (C) -----	12.2	-----
	VIII (N) -----	13.0	-----

<sup>a</sup> (N) Grew under normal conditions. (C) Kept at a constant weight.

These figures indicate that, while the weight was constant, the skin increased very slightly in weight.

Only the flesh, muscles, and fat of the body remain as the tissues which must have lost during the course of the experiments. The degree of this loss of flesh will be best recognized by considering the chemical composition of the different animals.

#### CHANGES IN THE CHEMICAL CONSTITUTION OF THE BODY.

The quantities of the different constituents are reduced to percentages of the live or body weight in order to facilitate this calculation. The absolute quantity of protein, fat, etc., is, of course, smaller in the dogs kept on a low diet than in the normally fed animals. This may not be absolutely correct in regard to the fat if the control animal was overfed during the course of the experiment. However, if the quantity of fat is far below the values which we find in the normal animals, there

<sup>17</sup> Das Wachstum des Kindes in "Kinderheilkunde in Einzeldarstellungen" (1898), 555.

can be no doubt that fat has been lost, since the changes in the general appearance of the animals are those which we regard as characteristic of a loss of fatty tissue.

The quantity of protein in the muscles of dogs II and III (experiment I) expressed as percentage of the live weights is slightly lower than the percentage of muscle protein in dog IV. The reduction in fat is considerably greater, the amount of this constituent, also calculated as a percentage of the live weight, in dogs II and III is only one-half the quantity which it is in dog IV. If we add the quantities of bone-ash, the protein, and fat of the muscles and bones, there remains of what I call the "body," a residuum consisting almost entirely of water, muscle-ash, and perhaps glycogen. This residuum amounts to approximately the same percentage (74 per cent) in the three animals.

Experiment III also gives information concerning the constituents of the "organs." The protein in the organs is not diminished in dog XI kept on a low diet, as compared with the other two dogs. The protein of the muscles, on the contrary, is greatly diminished. The fat varies somewhat in these animals. They did not receive the same quantities of food, and were not entirely alike, but it is clearly seen that number XI shows a considerably lower content of fat than do numbers VIII and XII. Fat, therefore, is not only lost from the "body," but also from the organs.

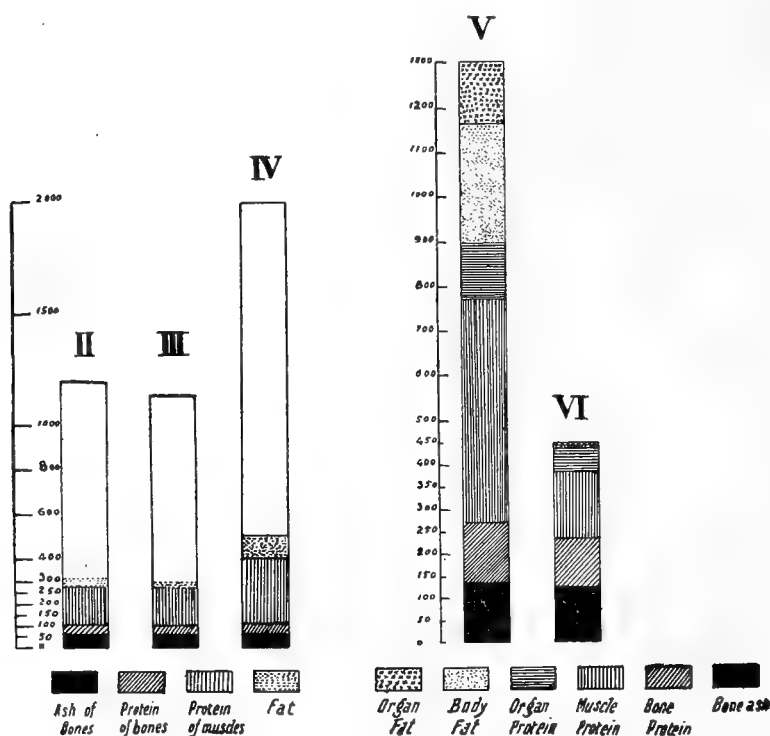


DIAGRAM 1.—Composition of dogs II to VI of Experiments I and II.

Experiment II illustrates this point better. Here again we see that the protein of the organs is not diminished, and for both animals we obtain values corresponding as closely as could be expected. The protein of the muscles is reduced in dog VI to one-half the amount which we assume was present at the beginning of the experiment. The fat is reduced to a small remainder, and has disappeared almost entirely from the bones. The protein in the bones is considerably higher than in all probability it was at the beginning of the experiment. This is not surprising when we recall that the skeleton grew at almost the normal rate.

All the experiments show that the fat of the body suffered the greatest loss. The greatest loss of fat was from the flesh and bone marrow. It was less severe in the organs.

The loss in body protein is large in the dogs kept at a constant weight, but not so great as the loss of fat. However, we must recall that the protein of the bones, the ossein, was not decreased, but actually increased. The organs, even of the animal dying of inanition, suffer no loss in protein.

There was a considerable loss of muscle protein in the animals kept at constant weight. For instance, the muscle protein in dog II amounted to only 5.4 per cent of the live weight, as compared with 10.7 per cent for the normal animal V. However, it is remarkable that not all the muscle protein which disappeared was lost from the body, for a portion reappeared in the form of bone protein. Therefore, the loss of total body protein is smaller than that of muscle protein alone.

Another question of great importance is whether or not the loss in fat and protein from the body and from the organs is fully compensated for by a corresponding increase in the bones. The mass of the bones, as just mentioned, increased considerably, but the quantity of newly formed bone-tissue is by no means sufficient to cover the entire loss in fat and protein. There must be something else in the body which has increased, for only if such an increase has taken place can we explain why the body weight, in spite of the tremendous decrease in flesh, has not diminished.

It is more than probable that water, the relative quantity of which has increased, is this constituent. A glance at the following diagram shows plainly that the water content of all parts of the body of dog VI is considerably greater than that of dog V, and also greater than that which we would regard as the normal water content. We can term the condition prevailing in dog VI one of general hydration (*Verwässerung*).

This increase in water content is not the same for all parts of the body. The greatest reduction in the amount of solids is found in the blood (estimated on the basis of the protein content). The blood

of dog number VI contained about one-fourth as much protein as that of dog V and of normal dogs (18 to 20 per cent).

The muscles contained only one-half of the normal amount of total solids.<sup>18</sup> The water content of the brain had also increased considerably. It will be remembered that the weight of the fresh brain of dog VI was 57 grams as compared with 52 grams for that of the full-grown control dog V. However, the water content was so much greater that the amount of total solids in the brain of dog VI was in reality smaller than that of number V. This process of hydration (*Verwässerung*) brings about the condition in which the weight of the brain of a dog kept at low diet is greater than that of a normal control animal.

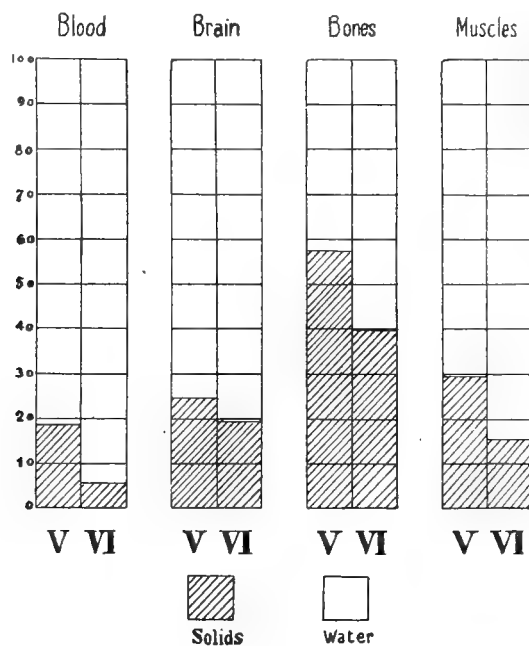


DIAGRAM 2.—Percentage of water and solids in blood, brain, bones and muscles of dogs V and VI of Experiment II.

The bones also show an increased water content in dog VI, as compared with dog V. However, in this case the percentage of ash in the bones is not diminished, and that of protein only very slightly so. Water in the starved bone really takes the place of fat in the normal one. These conditions are shown in diagram III.

The replacement of body substances by water in the different parts of the body, and the almost complete destruction of fat, demonstrates

<sup>18</sup> For this determination 25 grams of lean muscle from corresponding parts of the leg were selected, weighed and dried. The quantity of air-dried muscle was determined, then the dried material was powdered and the water content of this powder determined.



that all the animals on low diet were in a stage of starvation. Indeed, while their body weights remained constant, or were increased slightly, the animals were losing body substance, so that, while 1 gram of live weight of dog VI represented only 0.55 calories, the same weight of dog V represented 1.42 calories. This latter value agrees well with Rubner's findings (1 gram of dog equals 1.50 calories). Nearly two-thirds of the energy which dog number VI had stored at the time the experiment began must have been consumed during the experiment.

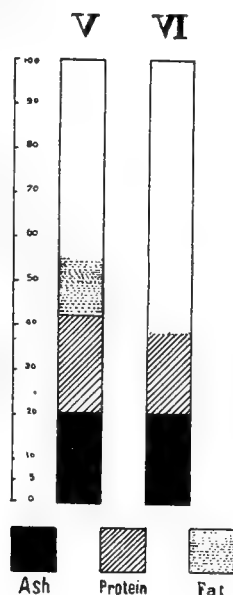


DIAGRAM 3.—Composition of bones of dogs V and VI of Experiment II.

It is quite interesting to compare the composition of the dogs which were kept on a low diet and the body weights of which remained constant or even increased slightly with that of adult animals which have undergone starvation.

During starvation of adult animals all parts of the body, even the skeleton, lose in mass. Skin, hair, and organs lose more than the muscles, but in our young dogs the muscles lose considerably more than the organs, which suffer scarcely any loss. Muscles, organs, brain, and spinal cord of a starved adult dog have the same water content as they have with normal dogs; the blood even becomes somewhat richer in solids. The converse is true with our dogs for there is a large decrease of solids, which is the most pronounced in the blood. However, in one respect the phenomenon is the same for starved young and for adult dogs, that is, the loss of fat from the muscles is comparatively greater than that from the organs.

## ENERGY REQUIREMENT AND FOOD CONSUMPTION.

Because the animals kept at constant weight during the experiment lost energy normally belonging to their bodies, we may conclude that the energy given in the food was less than was required for maintenance alone.

The energy requirement for the maintenance of a growing animal is equal to that for an adult of the same size. According to the surface law, we can find the amount of energy required for maintenance for dogs of any weight by means of the following formula:

$$E = 1039 \times 11.3 \sqrt[3]{W^2}, \text{ where } E = \text{energy and } W = \text{weight.}$$

Rubner has shown that a dog of about 6 kilos requires for maintenance 50 to 55 calories per kilo of body weight, a value 10 per cent below that given by the above formula.

In order to make the conclusion clear it will be necessary to compare the energy requirements of those dogs the body weights of which remained constant with the total number of calories actually given to them in their food.

The two dogs in experiment I, receiving from 80 to 85 calories, kept their weight constant at from 1,800 to 1,850 grams. There can be no doubt that these animals received considerably less than the required amount of energy, which should be from 150 to 160 calories. In spite of this fact they not only did not lose in weight, but even showed a slight tendency to increase. However, this experiment was comparatively short and we do not know how the animals would have behaved later on the same food.

In experiment III one animal, number XIV, of less than 1,000 grams, received from 70 to 75 calories and increased slightly in weight. Its requirement, according to the surface law, was from 115 to 120 calories. This animal died in ninety days, probably of inanition.

Dog XI of about 1,000 grams increased its weight slightly but constantly, while receiving from 90 to 95 calories, the requirement being from 125 to 130 calories. This animal began to lose weight, beginning with about the ninetieth to the one hundredth day and continued to lose when the energy intake was increased to 100 calories.

In experiment II a dog (VI) of more than 3,250 grams body weight received 140 calories, about one-half only of its requirement (250 calories), and within fifty days increased nearly 250 grams. As 270 calories were required for maintenance at this period, the intake was increased to 150 calories; then the body weight approximately remained constant, but still had a tendency to rise. In the next part of the experiment 135 and soon thereafter only 120 calories were given. Following this, the body weight began to fall. The animal then died of inanition.

The body weight in the last experiment remained at a standstill for

more than two hundred days in an animal of from 2,000 to 2,200 grams (dog A) which at first received 125, then 150, and later 170 calories, whereas 190 to 200 calories were required according to the surface law.

All these animals while receiving a considerably smaller quantity of energy than that required for maintenance, not only did not lose in body weight, but in the initial part of the experiment increased slightly.

The animals in the beginning of the experiment were well nourished with a fair storage of fat in their tissues. The growth of such an animal can not fully be stopped by restricting its food; for if we gave it the full-requirement for maintenance, certain parts of its body, especially the skeleton, would undoubtedly grow, thus increasing the weight of the animal. If we wish to keep such an animal from increasing in weight, we must starve it by giving so low a diet that the gain in weight, produced by the increase of certain parts of the body as an effect of their growth, is compensated by the loss in body substances used for maintenance in addition to the insufficient amount of calories taken in the food. The condition mentioned in the first lines of this paragraph is the one which we encounter in dogs II, III, XIV, XI, VI, and A at the beginning of the experiment. It is for this reason that we find such a great restriction of food necessary in order to prevent an increase in body weight, or to allow only a very slight one. In this period we are not able to suppress the growth by restricting the food, and constancy of weight does not indicate a cessation of growth.

However, these conditions change the longer the time during which this severe starvation lasts. If the greater part of the energy stored to give the reserve forces to the body is consumed, the animal, without losing in weight, becomes very much emaciated. If the low diet is continued, the animal finally loses somewhat in weight, and soon dies in a completely emaciated condition. This is simply because the animal does not have much more to lose. This explains the course of the experiments on dogs XIV and VI, in which case we could demonstrate plainly an entire loss of all reserve stuffs (fat) and a severe destruction of body proteins as well.

If instead of continuing the low diet, which initially was necessary to prevent an increase in weight, we follow it with sufficient food for maintenance or nearly that amount, the animal not only will be prevented from increasing in weight, but also from growing. This case is realized in experiment IV with dog A. In all probability, nearly all the reserve stuffs, all stored energy, in this animal were used up during the first period while the animal received only 110 calories, in the same manner as with dogs V or XI, where the fact was demonstrated by analysis.

We have seen by the foregoing considerations that, during the time of starvation, a considerable fraction of the energy required for maintenance is obtained from the energy stored in the body. However, this quantity

is very limited. For instance, in the case of dog II it can not have amounted to more than 20 or 25 calories per day; in that of dog XI, to 10 calories at most. The amount of energy which the animals could draw from their own bodies is hardly sufficient to give them all the energy required according to the surface law. Furthermore, we see that dog A maintained its body weight of about 2,200 grams with an intake of only 170 calories, whereas 190 were required, and yet we must assume that this animal had no further reserve stuffs to burn. I have already mentioned that the values for energy required for maintenance obtained by the general formula seem to be at least 10 per cent higher than those found, for instance, by Rubner in some of his experiments. On the basis of these values dog A, weighing 2,200 grams, receives sufficient energy from 170 calories, but in the case of dogs II and XI, the intake of energy plus the highest possible amount obtained from the body itself can scarcely cover the requirement. I conclude that emaciated animals show a low demand for energy. The opposite opinion generally prevails, namely, that an emaciated young animal (child) needs more energy per kilo for maintenance than a well-nourished one. (Lissauer, Schlossmann.)

In the Philippine Islands the prevailing temperature may have an influence. Emaciated animals in a temperate climate, where they are kept at from 15° to 20°, possibly may lose more heat and therefore require more energy for maintenance than in Manila, where the temperature rarely falls below 25°. At the time dog VI was most emaciated, the temperature varied between 28° and 35°. This point is worth mentioning because it may explain certain divergencies.

BIOLOGICAL CONSIDERATIONS CONCERNING THE SUPPRESSION OF GROWTH BY  
RESTRICTING THE FOOD.

In the course of our experiments we could distinguish two periods: *First period.* As long as there is a reserve of energy in the body, the animal draws on this and, while starving parts of the body, continues to grow. This "starvation" does not produce a loss in weight as it would with an adult animal, but is compensated, or even overcompensated for by an increase in the weight of the skeleton and by an increase of the water content of the body. (Verwässerung.) *Second period.* This begins when the animal has reached the last stage of emaciation, in which, if the intake of energy only meets the demand required for maintenance, no growth takes place and both weight and growth are at a standstill.

*During the first period, constancy or slight increase of weight indicates inanition, during the second period, cessation of growth.*

It is only possible to suppress growth entirely by restricting the food when an animal is so emaciated that it has no further reserve stuffs to draw on. From a biological standpoint there are two forces in a growing

animal which to a certain extent oppose each other, the tendency to grow and the tendency to maintain life. (Erhaltungstrieb.)

In the first periods of the experiments it appears that the tendency to grow in a young animal is greater than the tendency to maintain life. The further course of the experiments shows that the tendency to maintain life finally secures the upper hand. Therefore, the tendency to maintain life appears to be the greater biologic power. This observation is fully in accord with the results of investigations by Moreschi.<sup>19</sup> This author, at the suggestion of Ehrlich, studied the influence of a restriction of food on tumors in mice. He found that by a suitable restriction of food the growth of a tumor could be suppressed, that the tendency of the tumor to grow is not greater than the tendency to maintain life in the animal. Of course, this may depend on the malignancy of the tumor; in his experiments the power of the tumor-cells to attract material of nutrition was not greater than that of the normal tissue-cells.

We find similar conditions in our experiments: While the bones attract food material with great power, in order to grow, this tendency is finally overcome by that of the animal to maintain its life.

Some observations made by Waters and mentioned above, which lead to very similar conclusions, may be quoted here.

This author says that "ungrown animals that had been previously well nourished continued to increase in height and in width of hip for a considerable length of time, even though on a starving ration. Apparently, the animal organism is capable of drawing upon its reserve for the purposes of sustaining the growth process for a considerable time and to a considerable extent. Our experiments indicate that after the reserve is drawn upon to a certain extent to support growth, the process ceases and there is no further increase in height or in length of bone. From this point on, the animal's chief business seems to be to sustain life. This law applies to animals on a stationary live weight as well as to those being fed so that the live weight is steadily declining, and, indeed, to those whose ration, while above maintenance, and causing a gain in live weight, is less than the normal growth rate of the individual. Such an animal will, while gaining in weight, get thinner, because it is drawing upon its reserve to supplement the ration in its effort to grow at a normal rate."

We see from our experiments that the skeleton of all parts of the body has the strongest "tendency to grow." While the other portions not only do not increase, but lose constantly during the time when the animal maintains itself by burning its fat and muscle tissue, the bones increase in weight and size. Indeed, we find the paradox that while protein in the muscles diminishes in quantity, that of the bones increases. The brain, from what we have seen, also seems to have an intensive tendency to grow. The other internal organs also have doubtless a sufficient tendency, at least to maintain themselves. The muscles suffer a greater reduction than any other part of the body, and seem to have

<sup>19</sup> *Ztschr. f. Immunitätsforsch. u. exp. Ther.* (1909), 2, 651.

no real tendency to grow. They follow the skeleton whenever the nutrition is favorable enough to permit such growth, and the conclusion could be drawn that their growth is controlled rather by mechanical forces (traction) than by an internal force (tendency to grow).

#### ENERGY REQUIRED DURING GROWTH.

A short discussion of the behavior of the dogs which were amply fed is also necessary. For the purpose of calculating what fraction of the energy taken with the food was used for growth, we will take the average weight of the dog as a basis for the calculation of the energy required for maintenance. The excess of calories over this amount can be regarded as being used for the production of new body substances in a more or less economic way. As "optimal growth" we may term with Rubner the condition under which the greatest percentage of this excess of calories is transformed into new body substances. No one of our dogs probably was at this stage of optimal growth, but all of the animals were more or less overfed, and hence the number of calories used for the formation of 1 gram of new body substances was higher than at the stage of optimal growth.

I have calculated, in the way just described, the number of calories used for the production of 1 gram of new body substance for certain periods of our experiments. It seems advisable as a basis for such calculations to take periods as long as possible, in order to reduce the unavoidable error due to the daily variations of the live weight. The values obtained vary from about 1.6 to 4.6 calories (see the following table). The higher values, 3 to 4 calories, are found when the animal is amply fed and toward the end of an experiment when the animal is older. This will easily be understood if we assume that under these circumstances there is a relatively greater deposition of fat tissue, representing a higher caloric value.

*Number of calories used for the production of 1 gram of new body substance in dogs.*

Dog No.	In days.	From—	To—	Daily increase in weight.	Energy in food.	Energy for maintenance.	Difference.	Energy consumed for 1 gram growth.
		<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Calories</i>	<i>Calories</i>	<i>Calories</i>	<i>Calories.</i>
I-----	20	2,660	3,380	69	425	250	175	2.6
IV-----	10	2,290	2,670	28	340	210	130	4.6
IV-----	10	2,670	2,950	28	340	230	110	4.0
C-----	35	2,700	3,340	18	300	245	55	3.0
B-----	30	1,715	2,250	15.5	225	170	55	3.5
VIII-----	50	1,265	2,045	15.6	190	165	25	1.6
XII-----	50	1,572	2,532	* 19.0	215	185	30	1.6

Several authors (Oppenheimer,<sup>20</sup> Rubner, Graham-Lusk<sup>21</sup> and Wilson<sup>22</sup>) have attempted to formulate mathematical laws concerning the relation of the caloric intake to the increase in body weight. Rubner states that all young mammals, with the exception of man, in their first days of life need the same number of calories (4,808) to increase their body weight 1 kilo. This law would apply to a time when the food supply of the animal is controlled by nature, and we could understand a universal law under such conditions. However, it has already been shown that a number of Rubner's data are quite arbitrarily selected and that others, equally reliable, lead to different results.

Oppenheimer has observed that the growth in grams of normal, breast-fed children of the same age may be nearly proportional to the quantity of milk ingested.

This question has also been studied by Graham-Lusk, who, from his own experiments on suckling pigs performed in connection with Wilson, and from older experiments on dogs done by Rost,<sup>23</sup> has shown that, "during the normal development of the young of the same age and species, a definite percentage of the food (expressed in the caloric value) is retained for growth irrespective of the size of the individual."

While it is difficult to give a satisfactory explanation for this law from the standpoint of energetics, it seems to hold true in practice. For instance, Bamberg,<sup>24</sup> in a recent investigation on young pigs fed with the same milk, has obtained results from which we might also find a confirmation of Graham-Lusk's law:

Number of pig.	First five weeks of experiment.			
	Weight at start.	Increase	Quantity of milk.	$\frac{J}{Q}$
	Grams.	Grams.	Grams.	
C -----	1,963	5,004	4,621	1.08
D -----	1,743	3,557	3,469	1.02
E -----	1,850	2,632	2,344	1.12

In spite of the entirely different quantities of milk taken, there is a very surprising agreement between the quotients  $\frac{J}{Q}$  which indicate the increase in weight per unit of food (milk).

<sup>20</sup> *Ztschr. f. Biol.* (1909), 42, 147.

<sup>21</sup> *Science of Nutrition*, Philadelphia & London, 2. ed. (1909), 247ff.

<sup>22</sup> *Am. Journ. Physiol.* (1902), 8, 197, 212.

<sup>23</sup> *Arb. a. d. kais. Gsndhtsmte.* (1901), 18, 206.

<sup>24</sup> *Jahrb. f. Kinderheilk.* (1910), 71, 670.

I obtain figures confirming this rule from some of my experiments on amply fed dogs. If we compare the figures for a period of fifty days the following values are obtained:

Dog.	Calories.	Increase.		Increase.	Calories taken per gram increase.
		From—	To—		
		<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	
B.....	19,950	2250	3820	1,570	12.7
C.....	13,925	2220	3220	1,000	13.9
VIII.....	9,500	1265	2045	780	16.4
XII.....	10,750	1785	2623	838	15.6

However, if we compare the well and poorly nourished dogs of the same litter, the law does not hold. It seems clear that an animal gaining 1,000 grams during fifty days needs fewer calories for this gain than one gaining 1,000 grams in one hundred or one hundred and fifty days. In the first instance the animal needs to be maintained for only one-half the time as in the latter. Therefore, it seems nearly impossible to give any mathematical law, so long as the time factor can be varied freely.

INCREASE IN WEIGHT AS AN INDEX TO GROWTH WITH SPECIAL REFERENCE TO CHILDREN.

One of the most striking results of our experiments is the demonstration that lack of increase in weight in a growing animal does not indicate a lack of growth, but starvation, accompanied by loss of body substances.

This is of importance in practical pediatrics. We learn from it that a child which does not increase in weight or increases slowly is so under-nourished that part of its own body substances are being consumed. We can go even further in our conclusions. If a child does not present the weight which we have a right to expect at its age, assuming that it was born with a more or less normal weight, this child's body does not have the normal composition. It will contain a higher percentage of bones, a lower content of fat and muscle tissues, and a higher content of water and the caloric value of a unit of its body weight will be below that of a normal child. To feed such a child properly it is necessary first to attempt to replace water in its body by fat and protein. Therefore, it can use energy above the amount required for maintenance with-



out increasing in weight, or, for a certain increase in weight it will need more food than a normal child of the same weight. This explanation, based on our observation of "Verwässerung" as a consequence of continuous undernourishment, may give us the key to the understanding of a very remarkable fact recently reported by students of pediatrics and already mentioned in this paper. As Rosenstern<sup>25</sup> and others have shown and as I can demonstrate from my own observations, a child of a weight considerably lower than that which corresponds to its age will need a higher intake in calories per kilo for a normal increase in weight than either an infant of the same weight but younger, or one of the same age but heavier (normal weight).<sup>26</sup> This conclusion can best be shown by the following charts, which figure the food given and the weight observed in children of nearly the same weight but of different ages.

These observations are taken from milk-feeding stations established by the Bureau of Public Instruction in connection with public schools and conducted by Miss J. Jackson, under the supervision of the writer. I am indebted for the use of the following data to Miss Jackson who made up the milk daily for the children and observed them during the week, while only weekly inspections were made by the writer when the weights were taken.

Two characteristic examples are cited.

MARIA INOCENCIO.

From week—	To week—	Number of days.	Increase			Calories	
			From—	To—	Per day.	Per day.	Per kilo.
			<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>		
21	26	35	3,500	3,600	3	350-375	100-105
26	31	31	3,650	4,225	17	450-120	115-120
31	35	28	4,225	4,811	21	500	125

MIGUELA PRIEGA.

4	9	35	3,550	4,175	17	350-400	100
9	13	28	4,175	4,850	24	450-475	105

<sup>25</sup> *Deutsche med. Wchnschr.* (1909), 35, 295.

<sup>26</sup> Finkelstein and other authors advise that a child be given the number of calories that correspond to its age, irrespective of its weight.

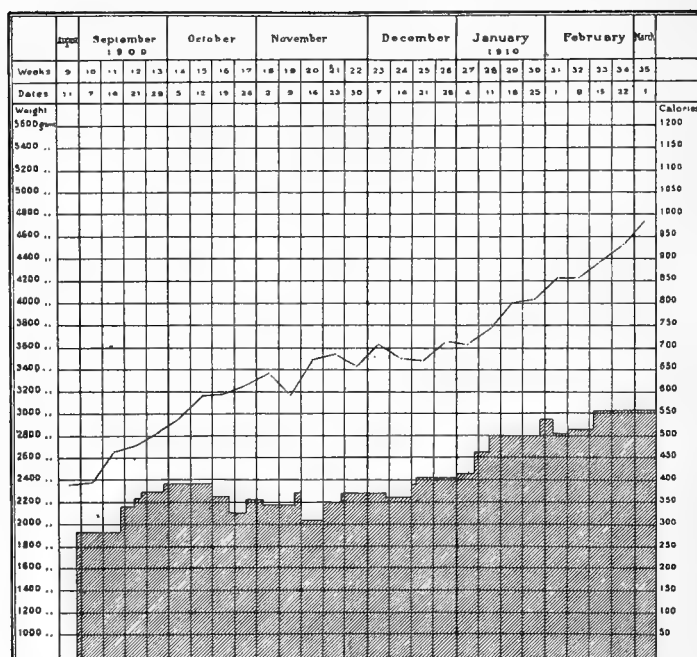


CHART 5.—Showing weight and food of Maria Inocencio.

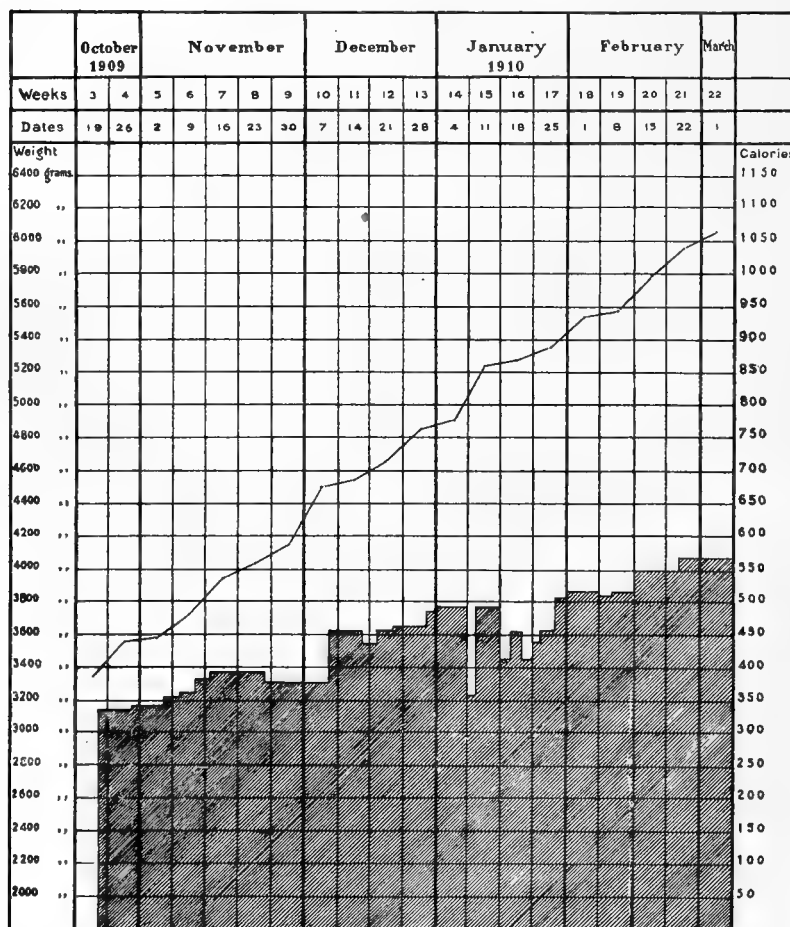


CHART 6.—Showing weight and food of Miguela Priega.

Maria Inocencio increased less than 5 grams per day, on a daily intake of from 100 to 105 calories per kilo, but 17 grams per day on a daily intake of from 115 to 120 calories per kilo, and she needed 125 calories per day to increase 27 grams per day. This child at the time of observation was from twenty to thirty weeks of age. The other child of the same weight, but only nine to fourteen weeks of age, with an intake of 95 calories per kilo increased about 17 grams per day, and with one of about 105 calories per kilo it increased 24 grams per day.

The question as to how far a continuous restriction in food, a constant undernourishment, may influence not only a single individual but entire nations and races, is doubtless very interesting and of unusual importance in the Philippine Islands. My experiments are not far enough advanced to justify conclusions concerning the possible influence of underfeeding upon offspring. The investigation of this question on mammals will necessarily require a long time. However, my work so far seems to indicate that a constant undernourishment will inhibit to some extent the normal development of the individual.

#### CONCLUSIONS.

The most important results of my experiments may be summarized as follows: A growing animal which receives only sufficient food to keep its body weight constant, or to allow a slight increase, is in a condition of severe starvation. If by a restriction of food the increase in weight is inhibited, the skeleton grows at the expense of other parts of the body, especially of the flesh. Most of the organs retain their weight and size, while the brain grows to reach its normal weight. The composition of the body—when at a constant weight—undergoes remarkable changes: Fat is consumed more or less entirely, the quantity of protein, especially of the muscles but not of the organs, is diminished and a great proportion of the body tissues is replaced by water; thus, this water and the increase of the skeleton together, replace the body materials lost. The caloric value of 1 gram body weight of an animal which has undergone such a process to its extreme limit may amount to only one-third of the normal value.

It is possible by supplying suitable amounts of food to maintain a dog in an emaciated condition, apparently in good health, and at the weight

of a puppy, for nearly one year, while its weight at the end of the year should be three times as great. If such an animal is thereupon fed amply, it fattens and rounds out, but does not reach the size of a control animal which from the beginning has been normally fed. It is unable to make good the growth suspended by the long restriction of food.

The "growth" principally depends on the tendency to grow possessed by the skeleton. The skeleton loses its capability of growing in more advanced age regardless of the size which the animal has reached.

I wish to thank Mr. Pio Valencia, formerly demonstrator in physiology, for his kindness in watching the animals when I was absent from Manila.

RECORDS OF EXPERIMENTS NOS. I-IV, SHOWING LIVE WEIGHT AND FOOD OF DOGS.

TABLE 14, EXPERIMENT I.—*Live weight and food of dogs I, II, III, and IV.*

Date.	Day of experiment.	Dog I.		Dog IV.		Dog II.		Dog III.	
		Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.
1909.									
January 20-----	1	1,435	124	1,430	124	1,419	80	1,390	80
January 25-----	6	1,465	236	1,570	236	1,410	125	1,310	110
January 30-----	11	1,710	285	1,730	285	1,480	130	1,330	110
February 4-----	16	1,995	(270)	2,090	(260)	1,575	95	1,510	(?)
February 9-----	21	Sick	290	2,100	305	Sick.	(?)	Sick.	110
February 14-----	26	2,235	340	2,290	330	1,705	85	1,735	110
March 19-----	31	2,475	370	2,560	350	1,840	85	1,715	90
February 24-----	36	2,660	340	2,670	330	1,810	80	1,720	85
March 1-----	41	2,800	380	2,760	350	1,865	80	1,750	80
March 6-----	46	3,100	380	2,950	355	1,910	80	1,780	80
March 11-----	51	3,220	380	3,060	355	1,830	80	1,780	80
March 16-----	56	3,380	380	2,990	355	1,950	80	1,800	80
March 21-----	61	3,560	425	-----	-----	-----	-----	-----	-----
March 26-----	66	3,850	425	-----	-----	-----	-----	-----	-----
April 1-----	71	4,250	425	-----	-----	-----	-----	-----	-----
April 6-----	76	4,410	425	-----	-----	-----	-----	-----	-----
April 11-----	81	4,420	425	-----	-----	-----	-----	-----	-----

TABLE 15, EXPERIMENT II.—*Live weight and food of dogs V and VI.*

Date.	Dog V.						Dog VI.				
	Day of experiment.	Weight.	Number of days.	Meat.	Starch.	Calories.	Weight.	Number of days.	Meat.	Starch.	Calories.
1909.				Gms.	Gms.		Grams.		Gms.	Gms.	
February 19.....	1	3,340	50	210	21	420	3,260	50	70	7	140
February 24.....	6	3,345					3,210				
March 1.....	11	3,805					3,320				
March 5.....	16	Sick.					3,340				
March 11.....	21	3,820					3,380				
March 16.....	26	4,000					3,410				
March 21.....	31	4,040					3,310				
March 26.....	36	4,280	50	170	17	335	3,310	50	75	75	150
March 31.....	41	4,400					3,345				
May 5.....	46	4,620					3,495				
April 10.....	51	4,610					3,430				
April 15.....	56	4,720					3,520				
April 20.....	61	4,850					3,545				
April 20.....	66	4,850					3,560				
April 30.....	71	5,020					3,540				
May 5.....	76	5,090	7	112	45	335	3,560	7	45	18	135
May 10.....	81	5,310					3,555				
May 15.....	86	5,340					3,510				
May 20.....	91	5,800					3,500				
May 25.....	96	5,370					3,500				
May 30.....	101	5,380					3,530				
June 4.....	106	5,320	13	120	48	360	3,500	92	40	16	120
June 9.....	111	5,370					3,590				
June 14.....	116	5,275					3,400				
June 19.....	121	5,285	10	140	56	420	3,480	92	40	16	120
June 24.....	126	5,260					3,210				
June 29.....	131	5,220					3,310				
July 4.....	136	5,290	77	160	64	480	3,375	3	50	20	150
July 9.....	141	5,280					3,330				
July 14.....	146	5,320					3,240				
July 19.....	151	5,310					3,150				
July 24.....	156	5,445					3,030				
July 29.....	161	5,610					3,000				
July 3.....	166	5,690					2,870				
July 8.....	171	5,815	3	50	20	150	2,880				
July 13.....	176	5,950					2,835				
July 18.....	181	5,805					2,835				
July 23.....	186	5,860					2,830				
July 28.....	191	5,780					2,950				
May 2.....	196	5,775					2,830				
September 7.....	201	5,750					2,850				
September 12.....	206	5,880	5,885				2,850	3	50	20	150
September 14.....	208	<sup>a</sup> 5,885					<sup>b</sup> 2,850				

<sup>a</sup> Two hundred and eighth day.<sup>b</sup> Two hundred and third day.

TABLE 16, EXPERIMENT III.—*Live weight and food of dogs VIII, XI, XII, and XIV.*

Day of experiment.	Date.	Dog VIII.		Dog XI.		Dog XII.		Dog XIV.	
		Weight.	Food.	Weight.	Food.	Weight.	Food.	Weight.	Food.
	1909.								
1	February 25	Grams. 585	10 days 130 calories	Grams. 760		Grams. 860		Grams. 782	
6	March 2	675	8 days 165 calories	800		942	21 days 225 calories	773	21 days 110 calories
11	March 7	720	4 days 200 calories	875	20 days 110 calories	1,150		780	
16	March 12	840		905		1,277		805	
21	March 17	990		950		1,400		866	
26	March 22	1,055	23 days 180 calories	975		1,482	22 days 205 calories	917	22 days 70 calories
31	March 27	1,125		980	25 days 90 calories	1,572		915	
36	April 1	1,177		973		1,650		935	
41	April 6	1,265		1,040		1,785		945	
46	April 11	1,342		1,089		1,845		923	
51	April 16	1,415		1,087		1,840		930	
56	April 21	1,500		1,044		1,912		944	
61	April 26	1,570	50 days 190 calories	1,122		2,052	52 days 215 calories	1,000	48 days 75 calories
66	May 1	1,671		1,185		2,179		1,020	
71	May 6	1,742		1,235		2,347		1,040	
76	May 11	1,820		1,270		2,460		1,070	
81	May 16	1,932		1,300		2,532		1,040	
86	May 21	1,982		1,340		2,605		1,015	
91	May 26	2,045	6 days 195 calories	1,306		2,623	5 days 225 calories	4915	
96	May 31	2,050		1,355	15 days 90 calories	2,760	10 days 230 calories		
101	June 5	2,100	12 days 180 calories	1,240		2,790			

106	June 10	2,105	32 days 240 calories	1,230	25 days 100 calories	2,780	30 days 250 calories	
111	June 15	2,225		1,325		2,790		
116	June 20	2,120		1,195		2,835		
121	June 25	2,120		1,160		2,865		
126	June 30	2,290		1,160		2,925		
131	July 5	2,297		1,070		3,028		
136	July 10	2,290				2,990		
141	July 15	2,345						
146	July 20							

<sup>a</sup> Killed one hundred and forty-sixth day; 2,375 grams.

<sup>b</sup> Killed one hundred and thirty-sixth day; 1,100 grams.

<sup>c</sup> Killed one hundred and forty-first day; 3,000 grams.

<sup>d</sup> Ninety-first day died; 915 grams.

TABLE 17, EXPERIMENT IV.—*Live weight and food of dogs A, B, C, and D.*

Date.	Day of experiment.	Dog A.		Dog B.		Dog C.		Dog D.	
		Weight.	Cal-ories per day.	Weight.	Cal-ories per day.	Weight.	Cal-ories per day.	Weight.	Cal-ories per day.
1909.		Grams.		Grams.		Grams.		Grams.	
August 1 -----	1	1,250	340	1,380	225	1,520	225	1,295	340
August 6 -----	6	1,340	340	1,450	225	1,580	225	1,360	340
August 11 -----	11	1,330	340	1,480	225	1,580	225	1,425	340
August 16 -----	16	1,465	300	1,520	225	1,640	225	1,485	340
August 21 -----	21	1,490	225	1,590	225	1,700	225	1,500	340
August 26 -----	26	1,505	225	1,605	170	1,745	150	1,515	225
August 31 -----	31	1,705	225	1,715	200	1,935	110	1,700	225
September 5 -----	36	1,770	110	1,780	225	1,890	110	1,840	225
September 10 -----	41	1,860	110	1,860	225	1,920	110	1,900	225
September 15 -----	46	1,950	110	2,020	225	1,940	170	1,990	170
September 20 -----	51	1,990	110	2,080	225	2,010	170	-----	-----
September 25 -----	56	1,935	110	2,150	250	2,040	200	-----	-----
September 30 -----	61	1,935	110	2,250	340	2,130	225	-----	-----
October 5 -----	66	1,960	110	2,500	400	2,320	250	-----	-----
October 10 -----	71	1,935	110	2,650	410	2,370	270	-----	-----
October 15 -----	76	1,935	110	2,830	410	2,490	270	-----	-----
October 20 -----	81	1,920	110	3,090	420	2,680	270	-----	-----
October 25 -----	86	1,850	135	3,180	440	2,700	300	-----	-----
October 30 -----	91	1,860	135	3,325	440	2,795	300	-----	-----
November 4 -----	96	1,900	135	3,525	440	2,935	300	-----	-----
November 9 -----	101	1,850	170	3,610	440	2,970	300	-----	-----
November 14 -----	106	1,915	170	3,720	460	3,095	300	-----	-----
November 19 -----	111	1,940	170	3,885	500	3,130	300	-----	-----
November 24 -----	116	2,045	170	4,010	500	3,220	300	-----	-----
November 29 -----	121	2,020	170	4,110	500	3,340	300	-----	-----
December 4 -----	126	2,030	170	4,335	500	-----	-----	-----	-----
December 9 -----	131	2,015	170	4,460	500	-----	-----	-----	-----
December 14 -----	136	1,940	170	4,490	500	-----	-----	-----	-----
December 19 -----	141	1,960	170	4,595	500	-----	-----	-----	-----
December 24 -----	146	1,995	170	4,820	500	-----	-----	-----	-----
December 29 -----	151	1,990	170	5,010	500	-----	-----	-----	-----
1910.									
January 3 -----	156	2,000	170	5,050	500	-----	-----	-----	-----
January 8 -----	161	2,010	170	5,020	500	-----	-----	-----	-----
January 13 -----	166	2,015	170	5,120	500	-----	-----	-----	-----
January 18 -----	171	1,950	170	5,100	500	-----	-----	-----	-----
January 23 -----	176	2,010	170	5,260	500	-----	-----	-----	-----
January 28 -----	181	2,050	170	5,270	550	-----	-----	-----	-----
February 2 -----	186	2,110	170	5,450	570	-----	-----	-----	-----
February 7 -----	191	2,040	170	5,510	570	-----	-----	-----	-----
February 12 -----	196	2,090	170	5,520	570	-----	-----	-----	-----
February 17 -----	201	2,180	170	5,605	570	-----	-----	-----	-----
February 22 -----	206	2,080	170	5,825	570	-----	-----	-----	-----
February 27 -----	211	2,230	170	6,090	570	-----	-----	-----	-----
March 4 -----	216	2,050	170	6,145	570	-----	-----	-----	-----

<sup>a</sup> Killed forty-ninth day.<sup>b</sup> Died one hundred and twenty-third day.



TABLE 17, EXPERIMENT IV.—*Live weight and food of dogs A, etc.*—Continued.

Date.	Day of experiment.	Dog A.		Dog B.		Dog C.		Dog D.	
		Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.
1910.		<i>Grams.</i>		<i>Grams.</i>		<i>Grams.</i>		<i>Grams.</i>	
March 9	221	2,100	170	6,140	570				
March 14	226	2,305	170	6,185	570				
March 19	231	2,315	170	6,335	570				
March 24	236	2,315	170	6,315	570				
March 29	241	2,310	170	6,370	570				
April 4	246	2,270	170	6,300	570				
April 9	251	2,220	170	6,400	570				
April 14	256	2,190	170	6,330	570				
April 19	261	2,165	170	6,290	570				
April 24	266	2,195	170	6,335	570				
April 29	271	2,150	170	6,250	570				
May 4	276	2,300	170	6,270	570				
May 9	281	2,300	170	6,350	570				
May 14	286	2,290	170	6,380	680				
May 19	291	2,220	170	6,360	680				
May 24	296	2,390	170	6,450	680				
May 29	301	2,350	170	6,420	680				
June 3	306	2,400	170	6,400	680				
June 8	311	2,440	170	6,460	680				
June 13	316	2,360	170	6,500	680				
June 18	321	2,320	170	6,500	680				
June 23	326	2,340	170	6,500	680				
June 28	331	2,350	170	6,690	680				
July 3	336	2,390	170	6,760	680				
July 8	341	2,400	170	6,800	680				
July 13	346	2,520	170	6,870	680				
July 18	357	2,450	170	6,800	680				
July 23	356	2,450	230	6,850	680				
July 28	361	2,510	280	6,850	680				
August 2	366	2,540	340	6,800	680				
August 7	371	2,650	340	6,700	680				
August 12	376	2,700	340	6,680	680				
August 17	381	2,790	340	6,700	680				
August 22	386	2,910	340	6,690	680				
August 27	391	3,000	340	6,550	680				
September 1	396	3,040	340	6,580	680				
September 6	401	3,220	340	6,700	680				
September 11	406	3,250	340	6,910	680				
September 16	411	3,225	340	6,835	680				
September 21	416	3,325	450	6,865	680				
September 26	421	3,470	450	7,000	680				
October 1	426	3,630	450	7,020	680				
October 6	431	3,715	450	7,005	680				
October 11	436	3,740	450	6,950	680				
October 16	441	4,245	680	<sup>a</sup> 7,060	680				
October 21	446	4,390	680	7,060	680				

<sup>a</sup> Both dogs receive equal amounts.

TABLE 17, EXPERIMENT IV.—*Live weight and food of dogs A, etc.*—Continued.

Date.	Day of experiment.	Dog A.		Dog B.		Dog C.		Dog D.	
		Weight.	Cal-ories per day.	Weight.	Cal-ories per day.	Weight.	Cal-ories per day.	Weight.	Cal-ories per day.
1910.		<i>Grams.</i>		<i>Grams.</i>		<i>Grams.</i>		<i>Grams.</i>	
October 26 -----	451	4,550	680	7,010	680	-----	-----	-----	-----
October 31 -----	456	4,690	680	7,080	680	-----	-----	-----	-----
November 5 -----	461	4,810	680	7,045	680	-----	-----	-----	-----
November 10 -----	466	4,925	680	7,125	680	-----	-----	-----	-----
November 15 -----	471	4,995	680	7,250	680	-----	-----	-----	-----
November 20 -----	476	5,130	680	7,340	680	-----	-----	-----	-----
November 25 -----	481	5,290	680	7,430	680	-----	-----	-----	-----
November 30 -----	486	5,300	680	7,400	680	-----	-----	-----	-----
December 5 -----	491	5,435	680	7,365	680	-----	-----	-----	-----
December 10 -----	496	5,395	680	7,320	680	-----	-----	-----	-----
December 15 -----	501	5,440	680	7,400	680	-----	-----	-----	-----

## ILLUSTRATIONS.

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### PLATE I.

- FIG. 1. Dog V of experiment II at the 175th day.  
2. Dog VI of experiment II at the 175th day.

### PLATE II.

- FIGS. 1 and 3. Dog A of experiment IV.  
2 and 4. Dog B of experiment IV.

### PLATE III.

- FIGS. 1 and 3. Dog A of experiment IV.  
2 and 4. Dog B of experiment IV.

### PLATE IV.

- FIG. 1. Dogs used in experiment IV.  
2. Some of the bones of dogs A and B used in experiment IV.

### DIAGRAMS.

1. Composition of dogs II to VI of experiments I and II.
2. Percentage of water and solids in blood, brain, bones, and muscles of dogs V and VI of experiment II.
3. Composition of bones in dogs V and VI of experiment II.

### CHARTS.

1. Variation in weights of dogs I to IV of experiment I.
2. Variation in weights of dogs V and VI of experiment II.
3. Variation in weights of dogs VIII, XI, XII, and XIV of experiment III.
4. Variation in weights and calories of dogs A to D of experiment IV.
5. Showing weight and food of Maria Inocencio.
6. Showing weight and food of Miguela Priega.



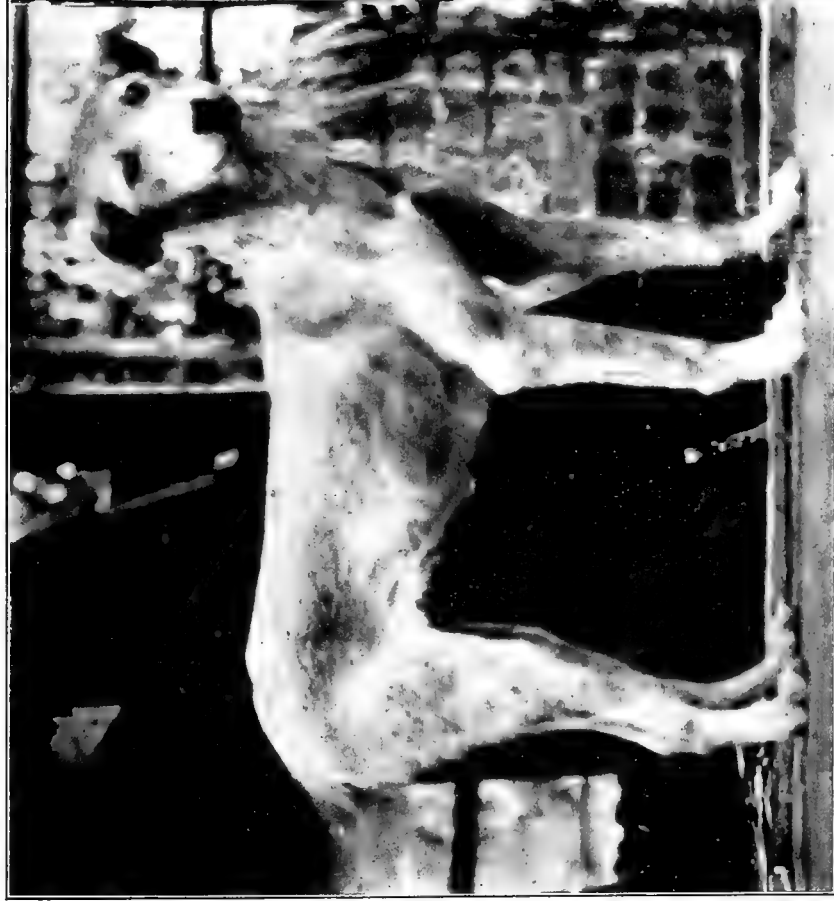


FIG. 1.



FIG. 2.

PLATE I.



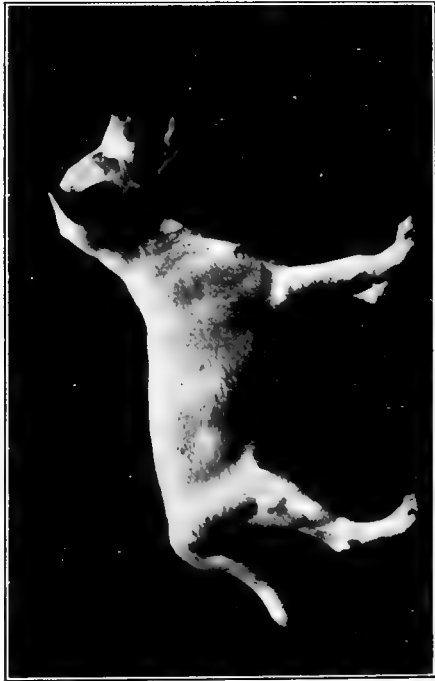


FIG. 1.

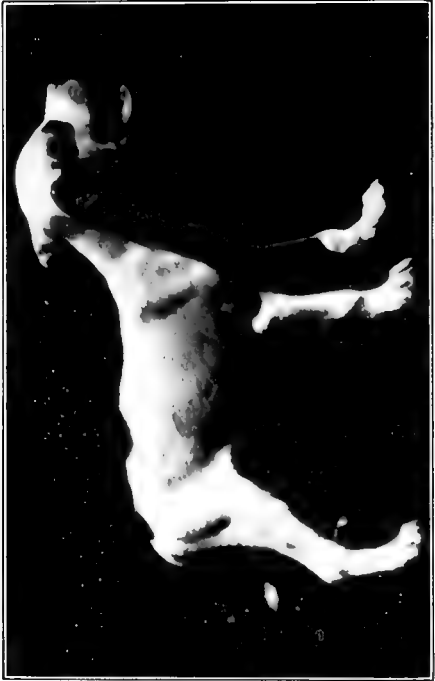


FIG. 2.



FIG. 3.



FIG. 4.

PLATE II.







FIG. 1.



FIG. 2.



FIG. 3.



FIG. 4.

PLATE III.





FIG. 1.

PLATE IV.

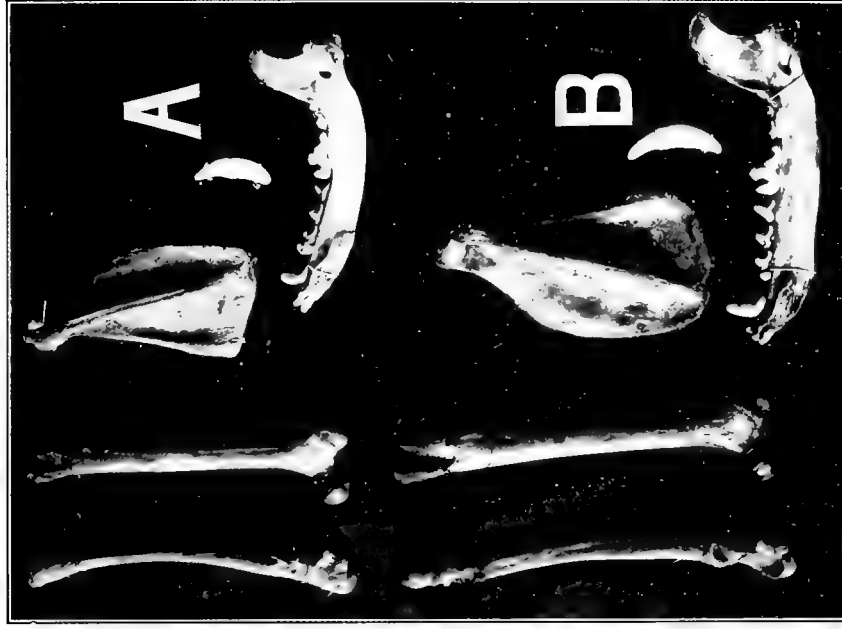


FIG. 2.



## INDICATIONS OF ACID INTOXICATION IN ASIATIC CHOLERA.

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By ANDREW WATSON SELLARDS and A. O. SHAKLEE.

*(From the Biological Laboratory, Bureau of Science, and the  
Pharmacological Laboratory, College of Medicine and Sur-  
gery, University of the Philippines, Manila, P. I.)*

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The position of the theory of acid intoxication in clinical medicine rests almost entirely upon the investigations in one disease, namely, diabetes. More or less prominent symptoms of acid intoxication may develop in some other conditions, such as starvation, the toxæmia of pregnancy, and after general anæsthesia, but the knowledge derived from these sources is of relatively minor importance when compared with that obtained from diabetes. However, there are certain features in Asiatic cholera which afford an interesting opportunity for the study of acid intoxication.

An increase in the daily excretion of sulphuric acid and of ammonia in the urine together with the presence of  $\beta$ -oxybutyric acid has been reported by Hoppe-Seyler.<sup>(1)</sup> In a concluding note of this same article, Quincke reports a case of cholera in which 30 grams of sodium citrate were given by mouth and by rectum in the course of three days, but during this period the urine remained acid. V. Terray, Vas and Gara<sup>(2)</sup> found a considerable increase in the excretion of sulphuric and of phosphoric acids and also of ammonia and acetone. Acetoacetic acid was often present.

Perhaps the most important feature in cholera which bears upon acid intoxication is the increased tolerance of patients for alkalis. The intravenous injection of sodium bicarbonate in relatively large quantities often fails to render the urine alkaline. In the interpretation of this tolerance, the anuria of cholera, following the excessive loss of fluid by rectum, offers a possible complication. The alkalis introduced into the body might be excreted by other channels, for example by rectum. However, if quantities of 30 to 60 grams were being excreted into the intestine one would almost expect that the kidney also would excrete at least enough alkali to change the reaction of the urine. Moreover, if the alkali is retained in the body during the period of anuria, there is the possibility that it might be neutralized by substances other than acids, such as serum albumins for example. Therefore, in Table I the intervals between the injection of alkali and the first secretion of urine have been included. Five control cases are also added.



TABLE I.—*Intravenous injection of sodium bicarbonate, etc.*—Continued.

Serial number.	Fifth injection.						Sixth injection.						Total amount of alkali.
	Alkali.			Urine.			Alkali.			Urine.			
	Interval between injections.	Per cent.	Amount	Interval after alkali.	Cubic centimeters.	Reaction to litmus.	Interval between injections.	Per cent.	Amount	Interval after alkali.	Cubic centimeters.	Reaction to litmus.	
	Hours.		Grams.	Hours.			Hours.		Grams.	Hours.			
1													20
2													50
3													25
5													20
6													20
7													20
9	22	1.5	15	1	130	Alkaline.							55
10	9	1.5	15	12	70	Acid.	12	1.5	30	12	120	Acid.	90
12													30
13													10
14													30
16													30
17													30
19													10
20													20
21													20

Control cases for Table I.

No.	Alkali.			Urine.					
	Per cent.	Cubic centimeters of solution.	Amount.	Interval after alkali.	Reaction to litmus.	Interval after alkali.	Reaction to litmus.	Interval after alkali.	Reaction to litmus.
			Grams.	Hours.		Hours.		Hours.	
1	1.5	300	4.5	1	Alkaline.	2	Acid.		
2	1.5	200	3.0	2	Acid.	5	Acid.	12	Acid.
3	0.5	400	2.0	1	Alkaline.	3	Acid.		
4	0.5	500	2.5	2½	Acid.	3	Alkaline.	5	Acid.
5	0.5	1,000	5.0	1	Alkaline.	3	Alkaline.	10	Acid.

Recovery took place in all of the cases which are recorded in Table I. There were also four fatal cases; two died during the first day in the hospital without excreting any urine and in the remaining two, the first samples of urine following the injection of alkali were lost. Of the sixteen cases which are recorded, there was but one in which the urine had an alkaline reaction; the quantities of sodium bicarbonate which were administered varied from two to eighteen times the maximum amount which was required to render the urine alkaline in the control cases.

As regards the increased excretion of ammonia in the urine, we have observed that occasionally the injection of rather large amounts of alkali does not reduce the ammonia out-put. A similar result may also occur in diabetes.<sup>(3)</sup>

*Suppression of urea.*—The first specimens of urine voided after a period of anuria are often found to contain subnormal amounts of urea. If the test is made with sodium hypobromite, it also shows that the content of ammonium salts as well may be relatively low in the first specimens. The explanations which suggest themselves may be considered under the two general heads, i. e. there may either be retention of urea by the organism or there may be a diminished production. In cases where there is suppression of urine, an acute nephritis is always present and one must consider the possibility of retention of urea on account of the kidney lesion. On the other hand, the nitrogen which is ordinarily transferred to the production of urea, might be diverted for the neutralization of acids. Lastly, a diminished production of urea might result from an impairment in the function of the urea-forming organs. A few data have been collected which have some bearing on these possible explanations.

*Excretion of urea by the kidneys.*—The possibility of retention of urea in the body was first considered. No determinations were made with the purpose of detecting an accumulation of urea in the blood or other tissues. Instead of this, urea was injected intravenously into patients who showed a well-marked suppression of urea, the object being to determine whether the lesions of the kidney were sufficient to prevent the excretion of urea, provided it were present in the blood. Previous determinations had shown that, in patients treated with sodium chloride, the urea, after a period of partial suppression, returns very gradually to normal. Only a limited number of cases were tested. In order to avoid a sudden spontaneous increase in the urea excretion, very severe cases were selected in which recovery, if it occurred at all, would be relatively slow. The urea in solid form was added directly to two liters of Ringer's solution and in every instance the injection was made intravenously. Relatively small amounts of urea were employed, the maximum being 10 grams. All of the cases showed a very acute nephritis in addition to the suppression of urea. The severity of the cases selected made it improbable that any spontaneous increase in the excretion of urea would take place. Four cases were obtained which were suitable for injection. The protocols are as follows:

The first patient (number 4) was admitted in partial collapse. During the first thirty hours in the hospital he received three intravenous injections of 2



liters each of Ringer's solution of which the third contained 10 grams of urea. The records of the excretion of urea are given in Table II.

TABLE II.—*Injection of urea, case No. 4.*

Interval between specimens.	Cubic centimeters of urine.	Per cent of urea.	Grams of urea.
<i>Hours.</i>			
	<sup>a</sup> 30	0.1	0.03
Injection of 10 grams of urea. <sup>b</sup>			
9	30	0.5	0.15
5½	50	0.6	0.30
9½	80	1.7	1.36
5	120	0.9	1.08
9	90	1.2	1.08
8	250	1.8	4.50
5	120	1.4	1.68
14½	10	0.1	0.01
Death after seventeen hours.			

<sup>a</sup> Preceded by anuria for twenty-seven hours.

<sup>b</sup> This injection was made four and one-half hours after the first specimen of urine was obtained. Catheterization showed no urine at the time of injection.

The volume of urine and the percentage and amount of urea are given, since the interpretation of the data is a little complicated because of the variation in the time intervals and the quantities of urine excreted. On the third day after admission, a fourth injection of two liters of Ringer's solution was given. Death occurred on the fifth day of the disease with symptoms both of toxæmia and uræmia. In the two and one-half days after the injection of urea a total of 10.1 grams of urea was excreted. Assuming that the percentage of urea would not have increased spontaneously, we may calculate the natural percentage for this period as 0.1, i. e. the per cent found before any urea was injected; on this basis we may deduct 0.8 gram as the amount which naturally would have been excreted leaving 9.3 grams as the increase due to injection. In addition to this amount there were also two specimens of urine which were lost by involuntary micturition, i. e. only 8 of 10 specimens were obtained. We may estimate, then, that about 90 per cent of the injected urea was excreted within two and one-half days.

A second case (number 11) required 8 liters of Ringer's solution intravenously during the stage of collapse. Two grams of urea were added to the third and 8 grams to the fourth injection. The period of reaction set in at the beginning of the fourth day and a fifth injection of two liters of Ringer's solution was given for its possible effect on the urine. Death occurred on the fifth day with symptoms of toxæmia and uræmia. During the first day, after the first injection of 2 grams a total of only 0.68 grams of urea was obtained and after the 8 gram quantity, only 2.6 grams were recovered although of the 4 voidings following the second injection one was involuntary and the specimen was lost. Hence in this case not more than one-third of the urea which we injected was recovered. The data are given in Table III.

TABLE III.—*Injection of urea, case No. 11.*

Interval between speci- mens.	Cubic centi- meters of urine.	Per cent of urea.	Grams of urea.
<i>Hours.</i>			
	<sup>a</sup> 70	0.1	0.07
13½	110	0.1	0.11
3	40	0.1	0.04
Injection of 2 grams of urea.			
4	60	0.1	0.06
13½	230	0.15	0.35
9	180	0.15	0.27
Injection of 8 grams of urea.			
5½	160	0.3	0.48
8	120	0.1	0.12
16	340	0.6	2.04
Death after six hours.			

<sup>a</sup> Preceded by anuria for twenty-eight hours.

In a third case (number 18) 5 grams of urea were added to the third injection of Ringer's solution. The patient died in uræmia, one and one-half days later. During this period a total of 1.7 grams of urea were recovered. The number of samples lost by involuntary micturition was unavoidably large, only about half of the specimens being obtained. The data are to be found in Table IV.

TABLE IV.—*Injection of urea, case No. 18.*

Interval between speci- mens.	Cubic centi- meters of urine.	Per cent of urea.	Grams of urea.
<i>Hours.</i>			
	<sup>a</sup> 100	0.25	0.25
Injection of 5 grams of urea. <sup>b</sup>			
3	60	0.5	0.30
6	50	0.2	0.10
9½	100	0.7	0.70
2½	15	0.11	0.02
5	80	0.25	0.20
2	85	0.3	0.25
Death after nine hours.			

<sup>a</sup> Preceded by anuria for nineteen hours.<sup>b</sup> This injection was made one and one-half hours after the first specimen of urine was obtained. Catheterization showed no urine at the time of injection.

In a fourth case, number 15, death occurred thirty-six hours after injection without any definite changes in the excretion of urea. Two specimens of urine were obtained during the stage of collapse, the urea falling from 0.6 per cent in the first to 0.05 per cent in the second. Then after a period of twenty-one hours of anuria, 8 grams of urea were injected. Two specimens of urine were

obtained before death. The first one of 20 cubic centimeters contained 0.6 per cent of urea. This was obtained one and one-half hours after the injection. A second specimen measuring 10 cubic centimeters was obtained fifteen hours later. It contained 0.25 per cent of urea.

As regards control patients, fatal cases have been frequently observed in which the variation in the urea content was very slight. A typical record of such a case is given in Table V. A patient dying in uræmia has been selected since more or less pronounced symptoms of uræmia were present in the four cases injected with urea.

TABLE V.—Control with sodium chloride.

Interval between speci- mens.	Cubic centi- meters of urine.	Per cent of urea.	Grams of urea.
<i>Hours.</i>			
—	<sup>a</sup> 75	0.2	0.15
13	100	.1	.10
13½	90	.15	.13
18	80	.3	.24
14	65	.2	.13
10	70	.4	.28
Death after twelve hours.			

<sup>a</sup> Preceded by anuria for forty-four hours.

Of the four cases injected with urea, there is one (Table II) in which a definite result was obtained. After the injection of urea, the percentage of urea increased eighteen-fold; then after a quantity equivalent to about 90 per cent of the amount injected had been excreted, the urea content fell to the same percentage that was found before the injection. This case would indicate that the suppression of urea is not always due to nephritis. The observations on this patient were carried out principally during the stages of collapse and reaction before symptoms of uræmia were prominent. The other three cases (numbers 11, 15 and 18) indicate that the behavior of this patient does not represent the usual result following the injection of urea, partly perhaps because of the difficulty of obtaining suitable cases for carrying out a complete test, or perhaps the urea in these three cases was used in the neutralization of acids before excretion could take place.

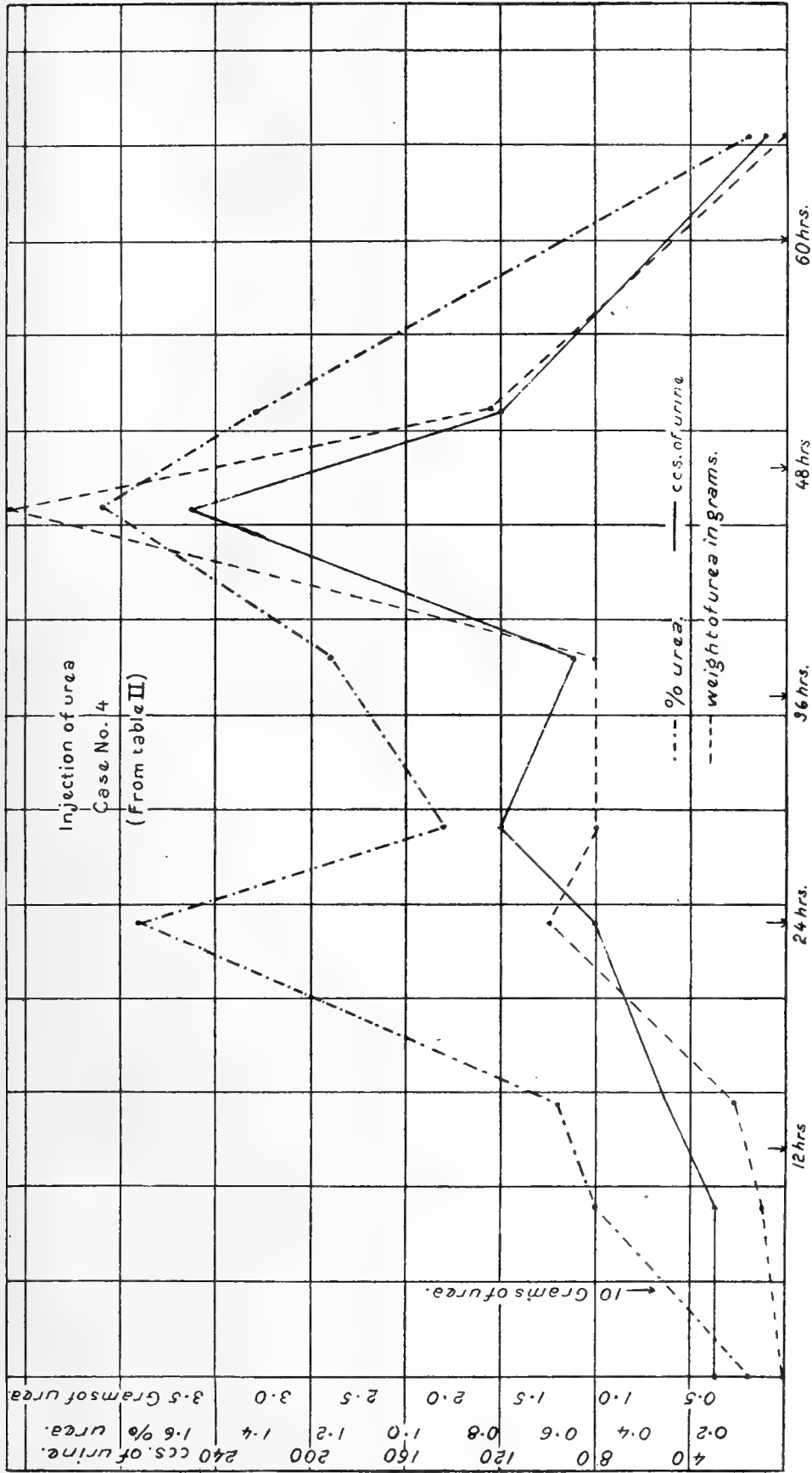
There is some evidence which indicates that the suppression of urea is not due to an impairment of function in the urea-forming organs. It was found in patients who were excreting only minimal amounts of urine that on the administration of bicarbonates the urea content sometimes rose almost to normal within a comparatively few hours. Thus, in one case, the percentage of urea rose from 0.05 per cent to 1.3 per cent in five hours. The data for this case are given in Table VI.

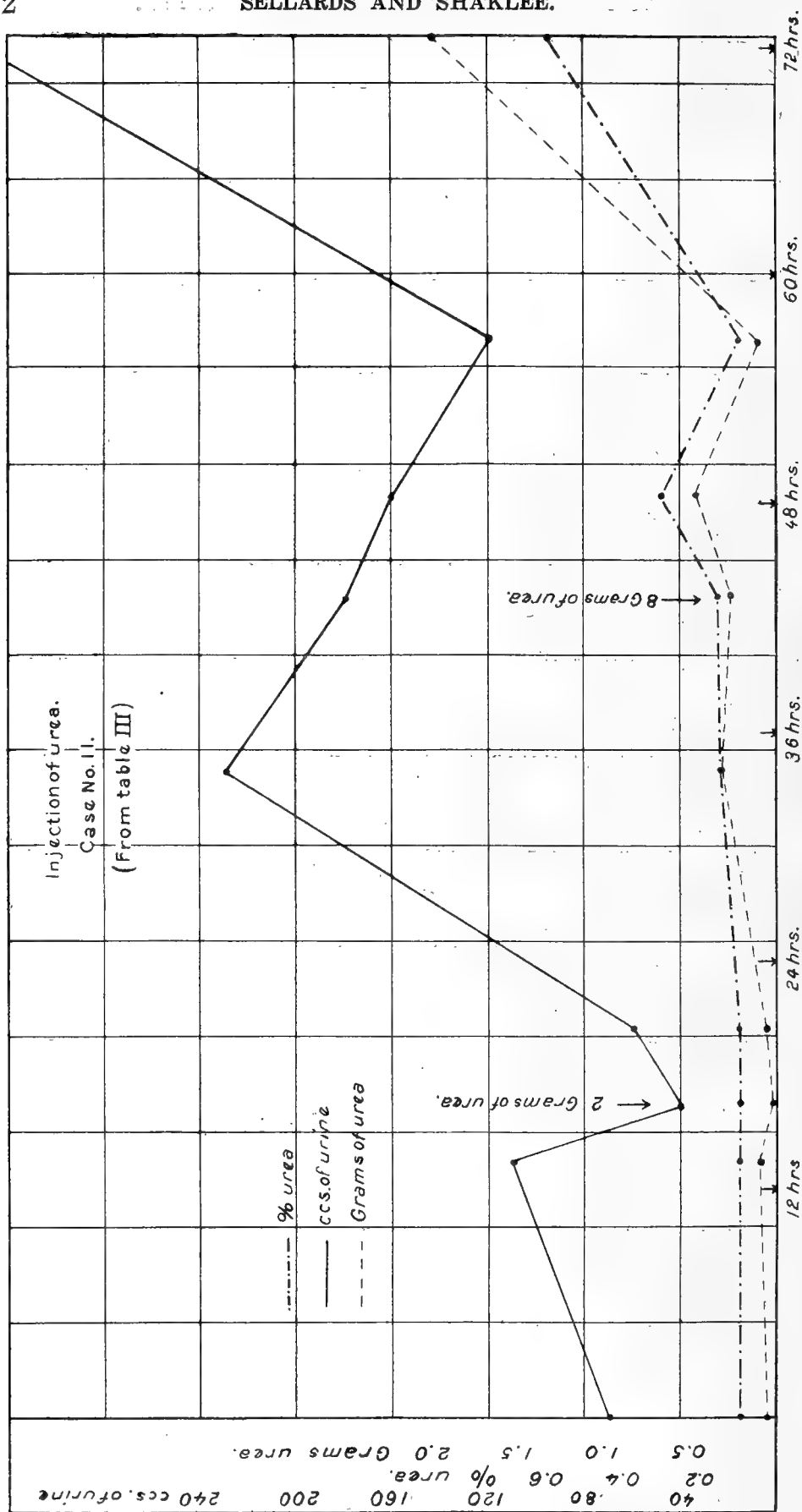
TABLE VI.—*Injection of sodium bicarbonate.*

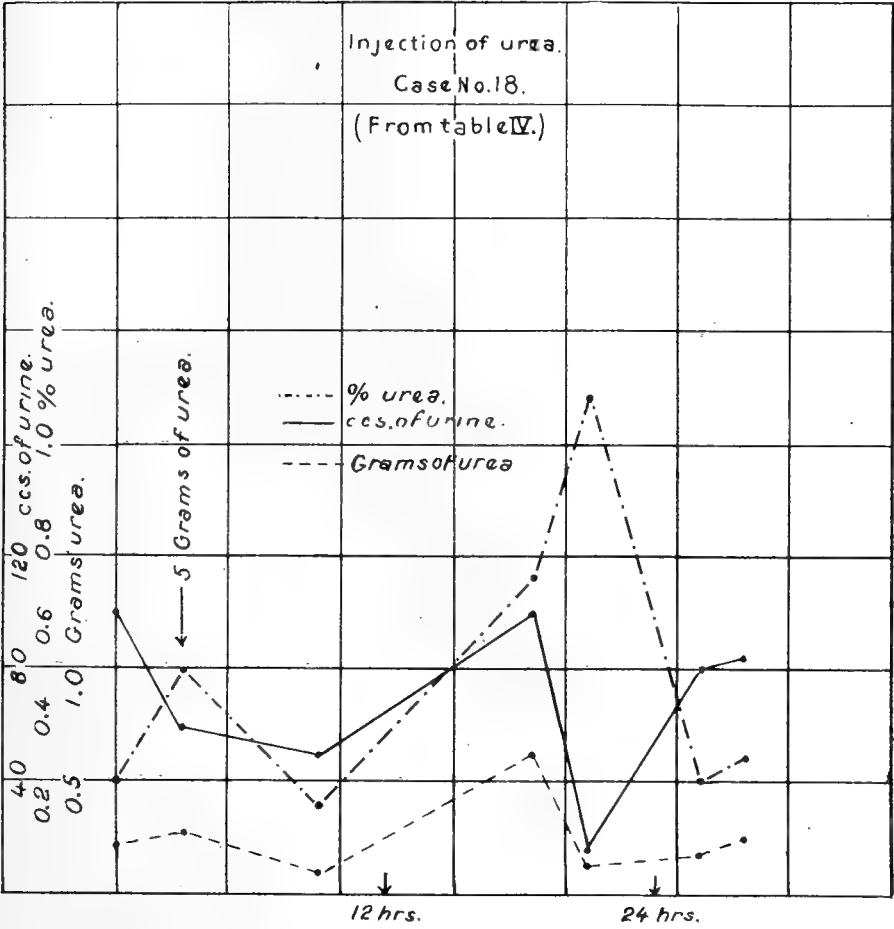
Interval between speci- mens.	Cubic centi- meters of urine.	Per cent of urea.	Grams of urea.
<i>Hours.</i>			
-----	15	0.05	0.0075
6½	6	0.05	0.003
8	2	0.05	0.001
Injection of 30 grams sodium bicarbonate.			
4	300	0.05	0.15
2½	110	0.5	0.55
1	150	0.8	1.2
1½	220	1.3	2.86
3	200	1.5	3.00
4	240	1.2	2.88
Recovery.			

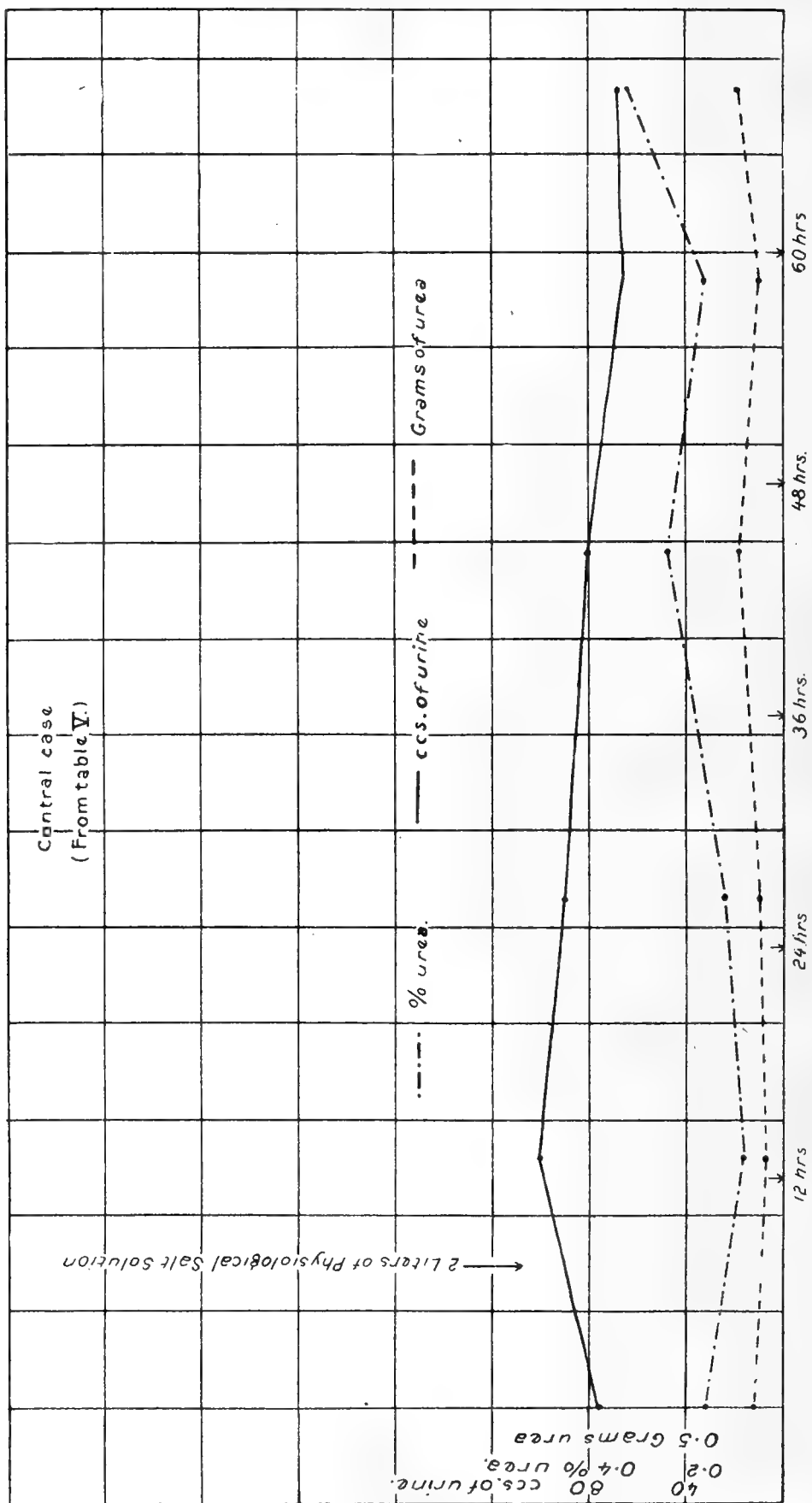
This might be interpreted as indicating that until the alkali was injected, nitrogenous material was being utilized for the neutralization of acids. However, there is one step in this explanation which is not clear. If the nitrogen neutralizes acids, one would expect to find ammonium salts in the urine on testing with sodium hypobromite, unless the neutralization took place in such a way that the resulting product failed to be excreted in the urine, or perhaps failed to react with the evolution of gas in the presence of the hypobromite.

For convenience, the results of the injections of urea and of sodium bicarbonate have been plotted in the accompanying charts. One of the urea cases (number 15) has been omitted as the data were incomplete. In two cases (numbers 11 and 18), the specimens of urine which were necessary for quantitative results could not be obtained; the qualitative changes, although somewhat suggestive, are not conclusive. The chart from Table II (case number 4) is especially interesting. Here the urea content following the injection of urea, rises from 0.1 to 1.8 per cent and then returns rapidly to its original point. The chart corresponding to Table VI gives the effect of the injection of sodium bicarbonate. Here the urea content rises from almost zero to normal and continues a normal course. In the control case, the amount and per cent of urea remain constantly low.

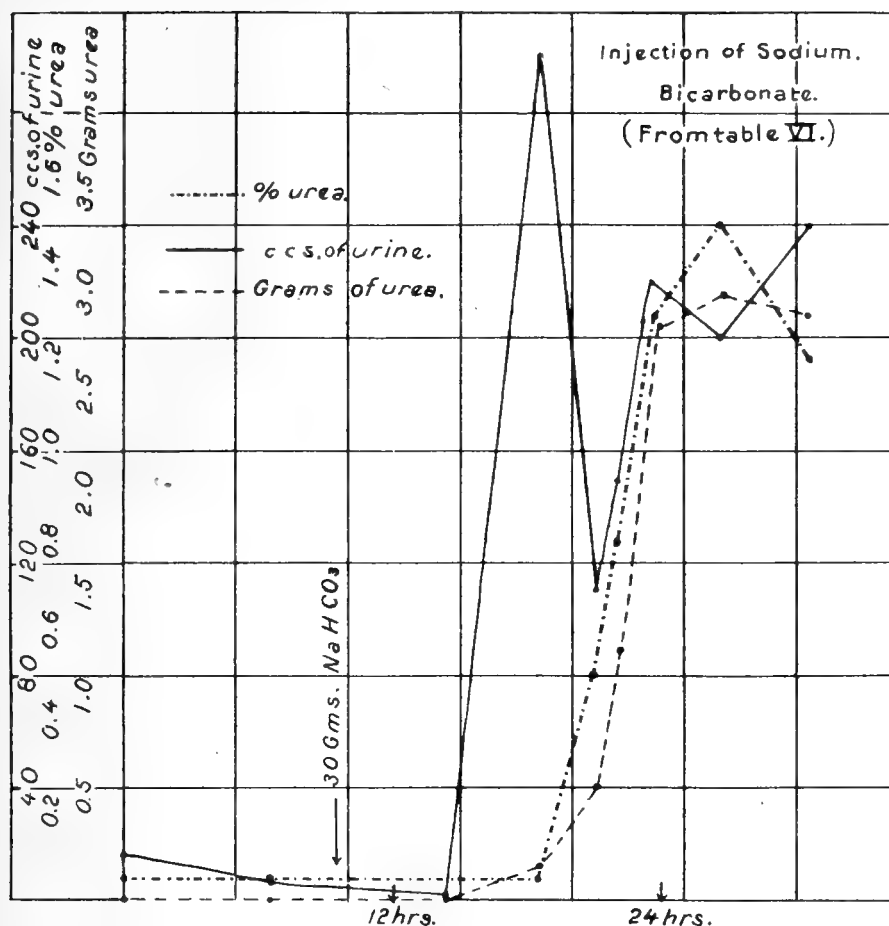












*Carbon dioxide content of the blood.*—In view of the decreased alkalinity of the blood which has been reported in cholera, it would naturally be of interest to determine its carbon dioxide content. In selecting a method for carbon dioxide determinations of the blood it must be remembered that none of the various procedures are free from error. The gravimetric method was used in the following determinations, according to the technique of Kraus. (4)

Blood was withdrawn with an ordinary syringe from a superficial vein of the arm below an Esmarch bandage and defibrinated with glass beads in a closed flask. The pressure throughout the apparatus was reduced to 16 centimeters. Approximately three to four times the theoretical amount of sulphuric acid was added using a 1 per cent solution instead of the more concentrated acid recommended by Kraus. After the addition of the acid, the apparatus was washed with air under the reduced pressure until the weight of the absorption bulbs was constant. Two absorption bulbs for carbon dioxide were used in order that the process might be carried out rapidly. The entire procedure was usually completed within three hours.

No determinations were made upon cases in collapse or in the stage of reaction, but only on those in which symptoms of uræmia were present. Two patients were available.

Case number 15 was tested on the fourth day of the disease, two hours before death. A total of 50 cubic centimeters of urine were excreted during the course of the illness. There were moderate symptoms of uræmia, and a typhoidal condition was also present. Case number 18 was tested on the third day of the disease, twenty hours before death. A total of 500 cubic centimeters of urine were excreted during the four days. There was only slight elevation of the blood pressure. The respirations were deep but the rate was not increased.

Determinations with this method on normal human blood gave results which closely approximated those obtained by volumetric methods, namely 40 to 50 volumes per cent of carbon dioxide. The specific gravity of normal blood (1.060) was used in calculating the volume of the sample of cholera blood from its weight. It is evident that this determination can represent only an approximation. However, the tendency of the error would lie in the direction of a high result rather than a low one. There was little opportunity for loss of carbon dioxide, but considerable care was required to prevent water from being carried over into the absorption bulbs. In these two patients there does not seem to be any reasonable doubt but that the carbon dioxide of the blood was definitely reduced below the normal.

TABLE VIII.—Carbon dioxide content of the blood.

Sample.	Weight of blood.	Increase in weight in CO <sub>2</sub> -absorption bulbs.		Total carbon dioxide.	Volume per cent of carbon dioxide.
		I.	II.		
Blank with water:	Grams.	Grams.	Grams.	Grams.	
I.-----		0.0009			
II.-----		0.0017			
Normal individuals:					
A.-----	15.10	0.0144	0.0003	0.0147	51
B.-----	17.47	0.0110	0.0023	0.0133	40
Cholera patients:					
No. 15-----	17.125	0.0062	0.0023	0.0085	26
No. 18-----	27.66	0.0065	0.0018	0.0083	16

In connection with these carbon dioxide determinations of the blood, it is interesting to note that Wittstock<sup>(5)</sup> has reported a decrease in the absorption of oxygen by the lungs and a decreased output of carbon dioxide in cholera.

#### EFFECT OF ALKALINE SOLUTIONS.

The results of alkaline therapy in diabetes have been of some value in the study of acid intoxication. Perhaps the simplest interpretation of these results is that, although an excessive amount of acid is usually present, yet it is probably not the sole ætiologic factor in the production of coma. The conditions in cholera in some respects are unusually favorable for observing the action of alkalies. For the most part, the patients are obtained after only a few hours of illness and before any symptoms of acid intoxication are present.

It has already been found that alkalies in large quantities produce a prompt excretion of urine in the stage of reaction. The most desirable period at which to commence the injection of alkalies and the most suitable concentrations were not definitely determined and therefore these questions have been given especial consideration in the following group of cases. In the main, two procedures suggest themselves. An apparently satisfactory plan would consist in the use of salt solution during the stage of collapse, followed by alkali in case the anuria persists during the stage of reaction. This has the disadvantage of requiring a considerable increase in the amount of fluid injected. For example, a patient receiving 5 to 10 liters of salt solution during the first day of collapse may require perhaps an additional five liters of alkali to start the excretion of urine. There are also certain theoretical objections to delaying the injection of alkali until the tolerance toward it has become well established. Such a delay would tend to favor the production of ammonium salts in the body. The toxicity of these salts in acid intoxication has been suggested by Mendel<sup>(6)</sup> and by Carlson and Jacobson.<sup>(7)</sup> Furthermore, if acids are allowed to accumulate, they may produce a permanent injury to the tissues which can not be remedied by the removal of the acids by neutralization. This suggestion has been offered in explanation of the merely temporary improvement after the use of alkalies in diabetic coma. A somewhat analogous condition may occur in cholera. It was noted in the uræmic stage, that the late administration of alkalies would cause a prompt excretion of urine and apparently prolong life for several days, although death ultimately took place. The free diuresis, following the bicarbonate injections when the stage of reaction appears, would afford better opportunities for elimination than could be effected by the intestinal tract alone.

However, during the stage of collapse when many liters of fluid are being lost by rectum no measures whatever have been effectual in producing excretion of urine. It is also a fact that the use of alkali during collapse has given no definite indication that it possesses any advantage over a neutral solution. Indeed the higher concentrations of 1 and 2 per cent can only be used for the first injection in carefully selected cases.

The following patients were treated with alkali with the object of determining the maximum concentration of sodium bicarbonate which could be used during collapse as a routine for all cases. Although a previous series showed that a fatal uræmia did not develop after large amounts of alkali, yet it is important to know definitely whether there is any increase in the number of deaths from other causes, that is, to know that patients who would have died in uræmia were not merely dying in collapse under alkaline treatment before the uræmic stage was reached. The possibility also has been suggested that uræmia causes only an apparent increase in the mortality, namely, that those cases which die in uræmia would terminate fatally from other causes if the course of the disease were not shortened by uræmia.

The patients available for this investigation were received at the hospital in the majority of instances rather early in the course of the disease only about one-half being in complete collapse. Several conditions indicate that the epidemic was at least moderately severe. During the period of investigation there were sixty-five deaths among untreated cases remaining in their homes, although the number of recoveries under such conditions is not available. There were a few individuals who died immediately on arrival at the hospital, or at the commencement of the first intravenous injection; two patients were received in an almost moribund condition and others repeatedly went into collapse, notwithstanding the frequent injection of salt solution. The disease in all instances was diagnosed bacteriologically by the staff of the Bureau of Science, the cholera vibrio being isolated in pure culture from the fæces and identified by agglutination reactions. Only uncomplicated cases showing typical clinical symptoms were selected; those presenting serious complications in addition to the cholera infection were not included. Thus, one case, admitted in pregnancy at full term, is omitted from the series, as well as another in which there was extensive tuberculosis. On admission to the hospital, the patients were divided into two groups of which one received the ordinary saline treatment and the other a solution containing 0.5 per cent of sodium bicarbonate. In the stage of reaction, the concentration of the bicarbonate was increased to 1.5 per cent in those cases in which suppression of urine persisted. As a routine the solutions were injected intravenously in 2-liter quantities, during the course of fifteen to thirty

minutes. In the stage of collapse, 4 liters of fluid were occasionally required for the first injection while in the stage of reaction 1 liter of 1.5 per cent sodium bicarbonate was sometimes sufficient.

#### PREPARATION OF RINGER-LOCKE AND OF THE ALKALINE SOLUTION.

For the control series an isotonic Ringer-Locke solution was prepared according to the formula: sodium chloride 0.9 per cent, potassium chloride 0.042 per cent, calcium chloride, crystallized, 0.024 per cent and sodium bicarbonate 0.03 per cent.

The sodium bicarbonate was added to determine whether these salts in the proportions in which they normally occur in the blood might not produce an effect similar to that obtained with larger amounts of the bicarbonate alone.

A solution of the preceding formula can not be sterilized by heat without conversion of the bicarbonate to the normal carbonate followed by subsequent precipitation of the calcium. Consequently the first three salts were added and the solution heated in the autoclave. The required amount of sodium bicarbonate was added in solid form immediately before the injection of the solution.

The formula was modified as follows for the alkaline injections during collapse: Sodium chloride 0.4 per cent, potassium chloride 0.042 per cent and sodium bicarbonate 0.5 per cent. The calcium was omitted on account of the insolubility of its carbonate. When the 0.024 per cent of calcium chloride was added in the presence of the 0.5 per cent of bicarbonate, a supersaturated solution occasionally would be obtained which would remain clear for a short period, but precipitation usually occurred after 20 to 30 minutes. An attempt was made to prepare the solution of sodium bicarbonate with a minimal conversion to the normal carbonate. The injection of sodium bicarbonate in aqueous solutions entirely free from normal carbonate would appear to be impossible since even at room temperature conversion to the normal carbonate takes place. Thus McCoy(8) found that in tenth molecular aqueous solutions at 25° C., 2.68 per cent of the bicarbonate immediately was converted to the normal carbonate and that equilibrium was not established until only 40 per cent of the bicarbonate remained unchanged. In stronger solutions the decomposition was much more rapid, e. g., in three-tenths molecular solutions, 77 per cent, and in molecular solutions, 86.2 per cent of the bicarbonate was decomposed at once. In view of these changes, the 0.5 per cent of bicarbonate was added in solid form to the sterilized solutions containing the sodium and potassium salts and the injection was made immediately without further heating of the solution. Samples of freshly prepared sodium bicarbonate were selected which were shown to be sterile when tested on ordinary culture media.

The 1.5 per cent bicarbonate solutions for injection during the stage of reaction were prepared without the addition of any other salt and were heated in the autoclave at 3 kilograms pressure per square centimeter for forty-five minutes, about 25 per cent of the bicarbonate being converted to the normal carbonate, under these conditions. For the preparation of 0.5 per cent bicarbonate solutions on a larger scale, it was found that an average decomposition of less than 3 per cent occurred when the solutions were heated in the autoclave in tightly stoppered bottles at a pressure of 3 kilograms per square centimeter for forty-five minutes, allowing the autoclave to cool to room temperature before opening to the atmosphere. The amount of normal carbonate in the solutions after sterilization was determined by titration at 0°C., against  $\frac{N}{100}$  hydrochloric acid in the

presence of phenolphthalein. The solutions were titrated within four days after sterilization. In two separate lots of solutions, the variations from this mean of 3 per cent were only slight. This amount of change is not greatly in excess of the conversion which takes place in the corresponding unheated solutions.

This solution was subsequently tested upon three typical cases in collapse and all recovered. The response from collapse was quite similar to that obtained with ordinary physiological saline solution. These three patients were sporadic cases occurring late in the cholera season, and for this reason they are not included in the group which is reported later.

Another factor was introduced in that some of the severest cases also received an anticholera serum. The reports concerning anticholera sera indicate on the whole that there is a certain minimal benefit to be derived from its use.(9, 10, 11) Its effect on the death rate is not sufficiently great to constitute any conclusive evidence of its value. Furthermore, if the use of alkalis affects only those cases which die in uræmia (15 per cent), then its influence on the death rate would not be very pronounced. By utilizing both methods of treatment it was thought that the combined effect might be great enough to show itself.

Aside from its having antitoxic properties, the serum perhaps might be of some minor value in protecting the corpuscles and the proteins of the blood from the action of the alkali; also it might aid in the retention of the injected fluid within the blood vessels, especially if the exudation of fluid through the vessel walls is dependent upon vital as well as physical phenomena.

The serum was prepared in a manner somewhat similar to that followed by Schurupoff.(10) Ten strains of cholera vibrios were tested and no marked differences were found in the minimal lethal dose of the killed cultures upon intraperitoneal injection into guinea pigs. The cultures were killed by adding sodium hydroxide to a thick emulsion of cholera vibrios in physiological saline solution.

Only freshly isolated strains of cholera were employed for the preparation of the serum, a new strain being obtained every month. The growth from 15 to 20 large agar slants was used for each injection, the slants each measuring about 3 by 8 centimeters. This growth was suspended in 20 to 30 cubic centimeters of salt solution and for the first injection the vibrios were killed by the addition of 2 cubic centimeters of  $\frac{N}{1}$  sodium hydroxide. Upon the addition of the alkali, the suspension changed from a limpid, opaque emulsion to a viscous, translucent solution. The viscosity was so great that dilution with an equal volume of salt solution was usually required in order to effect a thorough mixing. Further addition of the hydroxide diminished the viscosity of the fluid and apparently rendered it less toxic. The amount of sodium hydroxide was gradually decreased, until toward the end of the period of immunization, only one-fourth of original amount was used. This was not sufficient to kill the emulsion of vibrios, but their virulence for guinea pigs was diminished.

The injections were made intramuscularly at intervals of about two weeks over a period of four and a half months. Determinations were made of the protective power of the serum for guinea pigs against intraperitoneal inoculation of the vibrio emulsion killed with sodium hydroxide. The serum was tested before the injections were begun and at the end of the period of immunization, but no definite increase in this protective power could be detected. Three to 5 cubic centimeters of horse serum, either before or after treatment of the animal, when digested for thirty minutes with the minimal lethal dose of the cholera suspension (usually 1 to 2 cubic centimeters for intraperitoneal injection) were sufficient to completely protect guinea pigs of 300 grams. Sera of much higher efficiency have been obtained, notably that of Salimbeni<sup>(12)</sup> 0.002 cubic centimeter of which neutralized twice the lethal dose of cholera toxin. The behavior of the horse itself showed little evidence of immunity. The subcutaneous injections produced a local swelling and some rise in temperature. As the injections were continued there was only a slight diminution in this reaction. Finally, the minimal lethal dose by intravenous injection of the killed cholera material was determined upon normal horses. Three months after the last subcutaneous injection and after the horse had been under treatment for nine months, the intravenous injection of the minimal lethal dose, about 4 cubic centimeters, produced a fatal result in twelve hours.

The serum was used intravenously in 200 cubic centimeter quantities in 1 to 10 dilution in 0.5 per cent sodium bicarbonate solution. No more than two injections were made in any given case; therefore the maximum amount of the anticholera serum for any patient was 400 cubic centimeters. Favorable results have been reported with larger amounts, such as 1,040 to 1,390 cubic centimeters.<sup>(10)</sup> A very limited number of cases were treated with serum. Only those patients were selected in which the general symptoms were severe and the state of collapse was extreme. Six of these cases in the bicarbonate series were of this type. Two died in collapse without any definite response to the injections. The four remaining recovered, but without any pronounced differences from extreme cases which recover under sodium chloride treatment. However, the recovery of four of these six patients was unexpected and a control series with normal serum seemed advisable, but practically no cases were available. Only one patient was tested. He was admitted in complete collapse, and the toxæmia, though well marked, was not extreme. In all 600 cubic centimeters of normal horse serum were injected and a total of 12 liters of fluid. There was only a slight response to the injections. On the third day there were three moderately large hæmorrhages from the bowel, and death occurred on the fourth day.

Autopsy showed extensive œdema of the left lung with adhesions of the pleura. Multiple hæmorrhagic infiltrations extending to the serous coat were found in the small intestine. These areas measured about 1 centimeter in diameter; they were most numerous just above the ileo caecal valve and gradually disappeared in the upper fourth of the intestine.

The results, with the two groups of cases, showed that with Ringer's solution, only a small percentage of cases recovered after more than one day of anuria. In the bicarbonate group, a number recovered after one day of complete suppression of urine. The data are as follows:

Treatment.	Duration of anuria.	
	Less than 24 hours.	24 to 48 hours.
Ringer's.....	10	3
Bicarbonate.....	10	8

In dividing the patients into two similar groups, both the severity of the cholera symptoms and the general physical condition of the patients were considered. As nearly as could be determined there was no difference in either direction in the severity of the two series. The group treated with serum and bicarbonate represents those cases which went into complete collapse and in whom the symptoms of toxæmia were more or less prominent. Of the fifteen individuals treated with bicarbonate alone, five, and of the twenty-two control cases, twelve, were admitted in complete collapse.

The following classification has been used for estimating the effect of the bicarbonate solutions on the cause of death. Under collapse and enteritis are included those cases which die primarily from loss of fluid and also those which continue to live until the enteritis with its accompanying toxæmia is well developed. The uræmia of cholera, while differing from that of ordinary nephritis, is nevertheless characteristic. Two cases occurred in which symptoms both of uræmia and of the toxæmia of the cholera infection were present. Since each of these conditions may have been contributing factors in the cause of death, these are recorded as "intermediate."

The final results are given in the accompanying outline.

Treatment.	Number of cases.	Cause of death.			Total number of deaths.	Total number of recoveries. <sup>a</sup>
		Collapse.	Uræmia.	Intermediate cases.		
Bicarbonate and serum <sup>a</sup> .....	7	3	—	—	3	4
Bicarbonate.....	15	1	—	—	1	14
Total with bicarbonate.....	22	4	—	—	4	18
Control with Ringer's.....	22	5	2	2	9	13

<sup>a</sup> Including one patient receiving normal serum.



The patient who died under treatment with bicarbonate alone was a child eleven years old admitted in partial collapse.

Although in the control series there were only four deaths in which symptoms of uræmia were present, yet because of the constancy of uræmia, its absence is suggestive in the group of cases treated with bicarbonate and serum. Theoretically, the serum might prevent the development of uræmia if it could abort the infection.

There was no evidence to indicate that the serum was responsible for the absence of uræmia. In large epidemics where serum has been used extensively, nothing has been reported to show that the incidence of uræmia is lessened. The number of cases, treated without serum, namely fifteen, represent those which were less severe; but since even the mild cases are not always free from uræmia, this group would suggest that it was not the serum which prevented the development of this complication.

One patient (number 10), in the bicarbonate series, developed symptoms of uræmia. This case was admitted in complete collapse and responded poorly both to the injections of fluid and also to the serum, 200 cubic centimeters of which were used. During the first eighteen hours, 6 liters of 0.5 per cent bicarbonate were injected. At the end of the first day, during which time only 15 cubic centimeters of urine were obtained, the concentration of the sodium bicarbonate was increased, 1 liter of a 1.5 per cent solution being injected. Eight hours later, 140 cubic centimeters of urine were obtained by catheter, but this rate of excretion soon diminished and after nine hours an additional 15 grams of bicarbonate in 1 liter of water were given intravenously. After a twelve-hour interval only 70 cubic centimeters of urine were secured. The patient was not clear mentally, the restlessness was increasing, and the general condition was not good. A sixth injection of bicarbonate was given consisting of 2 liters of a 1.5 per cent solution.

As soon as the injection was well started, the patient complained severely of pain throughout the body and of cramps in the muscles. After the administration of one liter, there was considerable contraction and twitching of the muscles, which was especially noticeable in the extremities. The rigidity of the muscles did not entirely pass away until after eight hours. This is the only case in the series which developed muscular twitchings. A specimen of blood taken at that time showed a trace of hæmolysis, although none was observed after the use of 1.5 per cent sodium bicarbonate in a number of other cases. At this time, eight hours after the injection, no urine had been obtained and the symptoms of uræmia persisted. In view of the pronounced reaction which had followed the last injection it did not seem advisable to continue the injections of alkali. This case had received a total of 90 grams of sodium bicarbonate in two days. The patient had certainly passed the stage of collapse and as the anuria had not yielded to the injections of alkali, it apparently constituted a definite exception to the other cases. However, after an additional four hours 120 cubic centimeters of urine were obtained by catheter, and in the next twenty-four hours 1,200 cubic centimeters. The mental condition rapidly returned to normal after the excretion of urine commenced.

This group of patients showed definitely that the alkaline solutions were effective in starting the excretion of urine in the stage of reaction, whereas Ringer's solution had practically no permanent effect in severe cases.

The exact relation of acid intoxication and uræmia to each other is rather difficult to determine; there is a little evidence which suggests that an excess of acid leads to renal disturbance. Experimentally it has been found that mineral acids such as hydrochloric, give rise to nephritis and the acid intoxication accompanying a long-standing diabetes is associated with renal lesions. Lastly, there are certain evidences of an acid intoxication during the course of an ordinary uræmia. If it could be shown that the suppression of urine during the stage of reaction in cholera is due to an excess of acid, then the diuretic action of the alkali could be considered as specific and it would seem difficult to replace it by any of the ordinary diuretics. Early in the stage of collapse, when the anuria is due to loss of fluid by rectum, there is no evidence to show that in severe cases either the bicarbonate or the chloride solutions have any definite effect on the kidney. Apparently, no detailed examination has been made in regard to the action of diuretics in the stage of collapse, although free elimination by the kidneys in this stage might be of value.

The use of 0.5 per cent solutions of sodium bicarbonate during the stage of collapse was satisfactory in this group of patients for the majority of the cases. In two severe ones the response to the solution was very poor. It seemed a little better to discontinue the 0.5 per cent bicarbonate solution and change to Ringer's solution in those patients where a suitable response was not obtained. However, such cases apparently belonged to that group which fail to respond to any solution or any method of treatment. There was no evidence of any harmful effect in the use of bicarbonate in this series nor of any increase in the death rate from collapse or other causes. The early use of even relatively small amounts of bicarbonate appeared to lower the total amount which was needed to obtain secretion of urine. The rather large quantities of 50, 80 and even 90 grams, which are occasionally necessary were thereby avoided in a considerable proportion of cases. Excessively long periods of anuria did not occur. Thus, in Table I it will be seen that no patient who recovered showed complete suppression of urine for as long as forty-eight hours.

The cases treated with bicarbonate often appeared to improve rapidly and to recover more promptly than corresponding patients treated with Ringer's solution. However, this behavior was not constant. In one instance two patients were admitted in complete collapse and apparently were in almost duplicate conditions. The one receiving Ringer's solution recovered promptly, while the other responded very poorly to injections

of normal serum and 0.5 per cent bicarbonate, and died on the fourth day.

The death rate was low for the twenty-two cases treated with bicarbonate and serum; under less favorable circumstances, with cases received in the late stages of the disease, it would certainly be higher.

#### CONCLUSIONS.

The stage of reaction and uræmia in cholera and the acid intoxication of diabetes have the following features in common:

1. There is a well-marked tolerance for alkalies; as much as 90 grams in cholera and even 200 grams of sodium bicarbonate in diabetes may fail to render the urine alkaline. In certain stages of both diseases, sodium bicarbonate possesses pronounced diuretic properties.<sup>(13)</sup>

2. The relative and absolute amounts of ammonia in the urine are considerably increased in both diseases. The administration of alkalies, even in large amounts, sometimes fails to reduce the excretion of ammonia. In cholera, the urine frequently shows a pronounced diminution in the amount and percentage of urea; some evidence was obtained which suggests that the nitrogen may fail to be excreted as urea or ammonia, even when the organs which form urea are capable of performing their function and the kidney is able to excrete urea.

3. Preliminary tests indicate that there may be a definite reduction in the carbon dioxide content of the blood in the uræmia of cholera as well as in diabetic coma.

4. In both diseases, a diminished alkalinity of the blood has been reported.

5. The injection of alkalies in the late stages of either disease usually modifies the course without affecting the ultimate termination. The early administration of alkalies in cholera has been effective in preventing death from uræmia without any apparent increase in the number of deaths from other causes.

The exact significance of these analogies can be determined only by a thorough investigation. Acetone and acetoacetic acid have been noted in the urine of cholera cases but no excess of acid has been found which corresponds to the quantities of  $\beta$ -oxybutyric occurring in diabetes. Two forms of acid intoxication are distinguished by Naunyn, namely, a relative and absolute type. Loss of alkali from the body apparently may result from a pronounced diarrhoea, this loss giving rise to a relative acidosis. It also is conceivable that there may be an excessive quantity of acid present, resulting in the production of an absolute acid intoxication in cholera.

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# A STATISTICAL STUDY OF INTESTINAL PARASITES IN TOBACCO HACIENDAS OF THE CAGAYAN VALLEY, PHILIPPINE ISLANDS.\*

By DAVID G. WILLETS.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

TABLE I.—Summary of findings.

Examinations and infections.	Number.	Per cent.
Persons examined.....	4,278	
Persons infected.....	3,656	85.46
Persons infected with—		
<i>Ascaris</i> .....	2,653	62.04
Hookworm.....	2,326	54.37
<i>Trichuris</i> .....	342	7.99
<i>Oxyuris</i> .....	64	1.50
<i>Tenia</i> .....	59	1.38
<i>Hymenolepis</i> .....	5	0.12
<i>Strongyloides</i> .....	4	0.09
Trematodes <sup>a</sup> .....	1	0.02
Total infections.....	5,454	127.49

<sup>a</sup> Probably *Fascioletta ilocana* Garrison, 1908.

Upon the completion of the medical survey of the town of Taytay,<sup>1</sup> Rizal Province, in 1909, which was an effort to determine the health conditions in a representative Filipino community and which included the examination of the faeces of 1,000 persons, the Bureau of Health inaugurated a campaign to determine the frequency and medical importance of intestinal parasitism in other parts of the Island of Luzon with particular reference to the incidence and significance of hookworm infections. During the survey, 6,018 persons were examined at Las Piñas, Rizal Province; 2,594 at Tuguegarao, Cagayan Province; 802 at Santa Isabel, 3,310 at San Antonio, and 968 at Maluno, barrios of Ilagan, Isabela Province. The results obtained at the first three places have already been reported.<sup>2</sup> The present paper contains the findings at the last two places named.

\* Read at a meeting of the Manila Medical Society, January 9, 1911.

<sup>1</sup> *This Journal*, Sec. B (1909), 4, 207.

<sup>2</sup> Rissler and Gomez, *This Journal*, Sec. B (1910), 5, 267.

San Antonio and Maluno are tobacco haciendas. At the former place, 74.25 per cent of the population was examined; at the latter, 93.44 per cent. Therefore, the percentages of the various parasites found may be accepted as representing those present in the general population of the two haciendas.

In order that the work of the haciendas might not be too greatly interrupted at a time when there was a great deal to do in the fields, it was necessary to allow the people to save the specimens overnight; hence, the great majority of these were unfavorable for examination for the presence of amœbæ and flagellates, and no systematic search was made for the latter two classes of organisms. However, very few infections with these parasites were seen, so that it is believed they are infrequent at these two haciendas. The findings of Rissler and Gomez<sup>3</sup> in the Cagayan Valley are in accord with this impression and only one case of marked dysentery was seen; this probably was not amœbic since it responded to bismuth.

Nearly all of the persons examined were Ilocanos who migrated into the Cagayan Valley. There are included in the list the Spanish officials of the haciendas, 83 Ibanags composing *cabecera* number 9, and 58 Visayans composing *cabecera* number 33, of San Antonio. The findings among the Ibanags did not differ essentially from those among the Ilocanos, whereas the Visayans showed a high percentage of infection with the hookworm (77.59 per cent) and the whipworm (63.79 per cent).

Each hacienda is divided into districts which are subdivided into *cabecerias*. There are thirty-three such *cabecerias* at San Antonio and twelve at Maluno. Most of the houses are located on hills which are rocky, but which usually have a few trees. It appears that the selection of such sites for homes accomplishes a double purpose: It gives the tenants the advantage of available shade and places them above the water mark when the lowlands are flooded at various times during the rainy season. However, some of the houses are located in the lowlands. The variation in the location of the houses in the different *cabecerias* plays a rôle in the occurrence of the hookworm.

Several factors are acting upon the persons examined, excepting the officials, to lower their general vitality and render complex the problem of determining the effect upon them of intestinal parasitism. Marriage occurs early; child bearing is rapid; smoking is commenced at a tender age and is indulged in excessively throughout life; drinking of native whisky is commenced early; the diet is poor and consists of rice and maize, largely maize, with very little meat; and tuberculosis is common. Fortunately, malaria is rare.

The results obtained are based upon the examination of two thin cover-slip preparations of each specimen; it is understood that the findings of

<sup>3</sup> *Loc. cit.*

Rissler and Gomez were from the examination of one cover-slip preparation of each case. However, my results may be compared with theirs according to the testimony of a Filipino boy who made many of the preparations at Las Piñas, a large number of the microscopic examinations at Tuguegarao and Santa Isabel, and practically all of my own preparations, since no more faecal material was used in two of my preparations than in one of Rissler and Gomez.

RESULTS COMPARED WITH OTHER STATISTICAL STUDIES IN THE  
PHILIPPINES.

The results obtained are compared in Tables II and III, respectively, with those in other parts of the Philippines as to the number of infections found and the various parasites present.

TABLE II.—Percentages of persons infected and total infections in various parts of Luzon.

Authority and date.	Place.	Sex.	Exam-ined.	In-fected.	Per cent.	Total infec-tions, <sup>b</sup>	Per cent.
Garrison, <sup>4</sup> 1908	Manila	Mostly males	4,106	<sup>a</sup> 3,447	84.00	5,812	142.00
Garrison and Llamas, <sup>5</sup> 1909.	do	Women and children.	385	<sup>b</sup> 342	89.00	533	138.70
Garrison, Leynes and Llamas, <sup>6</sup> 1909.	Taytay, Rizal	Males and females.	1,000	<sup>a</sup> 959	95.90	1,726	172.60
Rissler and Gomez, 1910.	Las Piñas, Rizal	do	6,018	<sup>a</sup> 5,406	89.83	8,996	149.48
Do	Tuguegarao, Cagayan.	do	2,594	<sup>a</sup> 1,932	74.13	2,887	111.30
Do	Santa Isabel, Ilagan, Isabela.	do	802	<sup>a</sup> 692	86.28	927	114.34
Chamberlain, Bloombergh and Kilbourne, <sup>7</sup> 1911.	Baguio, Benguet	Adult males	119	<sup>b</sup> 110	92.50	209	174.00
Willets, 1911	San Antonio and Maluno, Ilagan, Isabela.	Males and females.	4,278	<sup>b</sup> 3,656	85.46	5,454	127.49
Total			19,302	16,535	85.66	26,544	137.52

<sup>a</sup> Protozoan findings included.

<sup>b</sup> Intestinal worms only.

<sup>4</sup> *This Journal, Sec. B* (1908), 3, 191.

<sup>6</sup> *Ibid.* (1909), 4, 207.

<sup>5</sup> *Ibid.* (1909), 4, 185.

<sup>7</sup> *Ibid.* (1910), 5, 505.

TABLE III.—Comparison of the various parasites reported in different parts of Luzon.

Authority.	Date.	Place.	Number exam- ined.	Ascaris.		Trichuris.		Hookworm.		Oxyuris.		Strongyloides.		Tenia.		Hymenolpis.	
				Number.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Garrison-----	1908	Manila, Bilibid Prison -	4, 106	1, 052	26.00	2, 426	59.00	2, 135	52.00	32	0.80	132	3.00	30	0.70	5	0.10
Garrison and Llamas.	1909	Manila, hospitals, etc -	385	182	53.22	300	87.60	46	13.45	2	0.60	2	0.60	1	0.30	0	0.00
Garrison, Leynes and Llamas.	1909	Taytay, Rizal Province.	1, 000	829	82.90	770	77.00	116	11.60	4	0.04	7	0.70	0	0.00	0	0.00
Rissler and Gomez.	1910	Las Piñas, Rizal Prov- ince.	6, 018	4, 647	77.21	3, 241	53.40	671	11.14	298	4.95	135	2.24	4	0.06	0	0.00
Do -----	1910	Tuguegarao, Cagayan--	2, 594	1, 907	73.55	672	25.90	208	8.01	68	2.62	0	0.00	13	0.50	19	0.73
Do -----	1910	Santa Isabel, Ilagan, Isabela.	802	486	60.59	50	6.23	364	45.38	10	1.24	0	0.00	11	1.37	6	0.74
Chamberlain, Bloombergh and Kilbourne.	1911	Baguio, Benguet-----	119	87	73.00	72	60.00	35	29.00	0	0.00	0	0.00	15	12.00	0	0.00
Willets -----	1911	San Antonio and Malu- no, Ilagan, Isabela.	4, 288	2, 653	62.04	342	7.99	2, 326	54.37	64	1.50	4	0.09	59	1.38	5	0.12
Total -----			19, 302	11, 843	61.36	7, 873	40.79	5, 901	30.57	478	2.48	280	1.45	133	0.69	35	0.18



In some of the studies the number of persons infected with intestinal worms alone is not stated as indicated in the table. It is probable that the findings at San Antonio and Maluno do not differ essentially from those in other parts of Luzon, excepting Tuguegarao, where approximately 10 per cent less of the population were infected than elsewhere.

It is noteworthy that the number of infections with intestinal worms per 100 persons examined was decidedly lower in the Cagayan Valley than in other parts of the island; this probably is due to the relatively low percentages of whipworm infections encountered in that locality.

The striking features of the findings at San Antonio and Maluno are the high percentage of persons infected with the hookworm and the low percentage with the whipworm (*Trichuris*). Rissler and Gomez found 45.38 per cent of the 802 individuals and 60.58 per cent of the adult males examined at Santa Isabel (which is also a tobacco hacienda) infected with the hookworm whereas 54.37 per cent of the 4,278 persons and 74.89 per cent of the adult males composing the present series harbored the parasite. That is, 8.99 per cent more of the general population and 14.31 per cent more of the adult male population was infected with the hookworm than heretofore reported for any section of the Philippine Islands. Garrison's series of 4,106 cases examined at Bilibid prison and which gave 52.00 per cent of hookworm infection, was composed almost entirely of adult males.

In my opinion, three factors are acting to produce a high percentage of hookworm infection at the haciendas, namely, the nature of the soil, the tobacco plants, and the occupation of the people. The soil is composed of clay with which sand is generously admixed, the tobacco plants furnish shade-conditions which are favorable for the propagation of the hookworm, and the cultivation of the tobacco keeps the people in the field daily during the greater part of the year. The belief that the infections are obtained in the fields is supported by the facts that the hookworm percentage increases rapidly when the age is reached at which work in the fields is begun,<sup>s</sup> that males, who are in the fields more than females, give a higher percentage of infection than the females, and that a greater percentage of persons are infected in the lowlands than in the uplands.

The findings in regard to the whipworm were quite as unexpected as those for the hookworm. Prior to the work in the Cagayan Valley, statistical studies had shown *Trichuris* to be very common in the Philippine Islands, Garrison and Llamas finding as high as 87.60 per cent of 385 women and children of Manila infected with it. Rissler and Gomez found 25.90 per cent of the persons examined at Tuguegarao and 6.23 per cent of those examined at Santa Isabel to be infected with the same parasite. (See Table III.) At Maluno only 4.75 per cent

<sup>s</sup> That is, about 7 years.

and at San Antonio 8.94 per cent of those examined harbored the whipworm. At the latter place the percentage was raised because of the presence of some Visayans who had been in the valley about one year and many of whom were infected with the parasite in question and because the inhabitants of certain *cabecerias* made frequent visits in Ilagan *Central*.

The low percentage of whipworm infection probably is due to a lack of introduction of this parasite in great numbers in the haciendas. *Trichuris* and *Ascaris* have thick-shelled ova and high percentages of these parasites are not infrequently found in a given community. The conditions favorable for the propagation of the one are, in a general way, favorable for the other. Now, the round worm is the parasite which occurs most frequently at the two haciendas. That the lack of introduction in sufficiently great numbers accounts for the relative infrequency of the whipworm is supported further by the fact that the neighbors of the Visayans to whom reference has been made and persons living near Ilagan *Central* show a higher percentage of infection with this parasite than do those who live at a distance.

Trematode ova in the stool of a boy 13 years of age appeared to be those of *Fascioletta ilocana* Garrison. Other than this, no unusual infection was seen.

#### COMPARISON OF FINDINGS AT SAN ANTONIO AND MALUNO.

Practically all of the people at the haciendas are of the same origin, and since they are all engaged in the same sort of labor in the same kind of soil it was to be expected that there would be but slight variations in the findings at the two places. This proved to be true.

Table IV shows the percentage of persons at the two haciendas who harbored single, double, triple, and quadruple infections and also the number per 100 persons examined. The great majority of the single infections was with the hookworm, or *Ascaris*; of the double, hookworm and *Ascaris*; and of the triple, hookworm, *Ascaris* and *Trichuris*.

TABLE IV.—Percentage of persons harboring intestinal parasites at San Antonio and Maluno.

Place.	No. ex- am- ined.	Infected.		Infections.								Total infections	
				Single.		Double.		Triple.		Quadru- ple.			
		Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
San Antonio...	3,310	2,819	85.16	1,529	46.19	1,133	34.23	151	4.56	6	0.18	4,272	129.06
Maluno .....	968	837	86.47	509	52.58	311	32.13	17	1.76	0	0.00	1,182	122.11
Total.....	4,278	3,656	85.46	2,038	47.64	1,444	33.75	168	3.93	6	0.14	5,454	127.49

Table V shows the relative frequency of the various parasites found at the two haciendas. The variations practically are negligible, excepting in the case of *Trichuris* which was found nearly twice as frequently at San Antonio as at Maluno; this is accounted for by the presence at the former place of the Visayans and the proximity of certain *cabecerias* to Ilagan Central. No infections with *Hymenolepis* or *Strongyloides* were found at Maluno.

TABLE V.—Relative frequency of the various parasites found at San Antonio and Maluno.

Place.	Num-ber exam-ined.	Infected.		<i>Ascaris</i> .		Hookworm.		<i>Trichuris</i> .	
		Num-ber.	Per-cent.	Num-ber.	Per-cent.	Num-ber.	Per-cent.	Num-ber.	Per-cent.
San Antonio-----	3,310	2,819	85.17	2,082	62.90	1,788	54.02	296	8.94
Maluno-----	968	837	86.49	571	58.99	538	55.58	46	4.75

Place.	<i>Oxyuris</i> .		<i>Tænia</i> .		<i>Hymenolepis</i> .		<i>Strongyloides</i> .		Total infections.	
	Num-ber.	Per-cent.	Num-ber.	Per-cent.	Num-ber.	Per-cent.	Num-ber.	Per-cent.	Num-ber.	Per-cent.
San Antonio-----	51	1.54	45	1.36	5	0.15	4	0.12	*4,272	129.06
Maluno-----	13	1.34	14	1.45	0	0.00	0	0.00	1,182	122.11

\* One trematode infection included.

Because the findings at the two places differ so slightly, they will be considered together in the following pages, excepting under the subject of geographic distribution, when conditions at San Antonio alone will be dealt with.

#### SEVERITY OF INFECTIONS.

The severity of the infections is measured by an impression of the number of ova seen in the specimens. Many of those with *Ascaris*, especially the ones occurring in children, were heavy, and those with *Trichuris*, *Oxyuris*, *Hymenolepis* and *Strongyloides* were light excepting a few cases of *Trichuris*. In one case the ova of the hookworm were very numerous, in a few instances not exceeding 15 ova per cover slip preparation were seen, while in the vast majority of cases, from 1 to 3 ova were present.

It is surprising to find practically only mild infections with the hookworm in a district where the parasite is found in over 50 per cent of the population. It has occurred to me that the flooding of the lowlands during the rainy seasons may be considered in this connection. Experiments have shown that fresh eggs of the hookworm die if they are placed in water, or if the culture medium (sand, or animal charcoal) is kept

too moist. The same results are secured with the rhabditiform embryo of the parasite. On the other hand, the filariform embryo will live for a considerable time in water. Now the lowlands of the haciendas are flooded nearly every year. Sometimes they are flooded three or four times in one year and they remain so for three or four days at a time. It is possible that during the floods many of the eggs and embryos are killed, and that many others are washed away. If this were true it would tend to lessen the percentage of persons infected, and the severity of the infections with this parasite. It is also probable that the heavy rains themselves tend to clean the infested soil yearly. These suggestions are offered only as possibilities, not facts. In my opinion, not less than 95 per cent of the hookworm infections seen were distinctly mild in degree. If this is correct, it seems necessary to believe that some factor or factors are at work to cleanse the infested soil from time to time.

## SEX.

The infections with *Hymenolepis* and *Strongyloides* are too few to admit of comparison. Males were found to harbor the hookworm and *Tania* more frequently than females, whereas more females than males were infected with *Ascaris*, *Trichuris* and *Oxyuris*, as shown in Table VI.

TABLE VI.—Sex distribution of infections.

Sex.	Num- ber exam- ined.	Infected.		<i>Ascaris</i> .		Hookworm.		<i>Trichuris</i> .	
		Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Males -----	2,290	1,999	87.29	1,349	58.91	1,432	62.53	179	7.82
Females -----	1,988	1,657	83.35	1,304	65.59	894	44.97	163	8.20

Sex.	<i>Oxyuris</i> .		<i>Tania</i> .		<i>Hymenolepis</i> .		<i>Strongy- loides</i> .		Total infections.	
	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Males -----	23	1.00	35	1.53	3	0.13	3	0.13	3,024	132.05
Females -----	41	2.06	24	1.21	2	0.10	1	0.05	2,429	122.18

It will be noted that in the total infections present there were 132.05 per 100 males as against 122.18 per 100 females.

## AGE.

The distribution of the parasites according to age is given in Tables VII, VIII, and IX. *Ascaris* was found to be more frequent in children than in adults, the highest percentage of infection (85.19) being in girls between 3 and 4 years old. Commencing with the group 7 to 9

years of age, there was a decided fall in the frequency of this parasite as age advanced, excepting a slight rise in females over 50 years old. *Trichuris* showed but slight variations as to sex and age. It was found more frequently in persons over, than in those under 15 years old. Infections with *Tænia* were met with more frequently in males over 50 years old, all of those with *Hymenolepis* occurred in persons under 16 years of age and *Oxyuris* was found oftener in individuals under 15. The hookworm occurred more frequently in males than females in corresponding age groups, excepting the small group of infants less than one year old.

TABLE VII.—Age distribution of infections.

Age (years).	Number examined.	Infected.		<i>Ascaris</i> .		Hookworm.		<i>Trichuris</i> .	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1 .....	20	3	15.00	3	15.00	1	5.00	0	-----
1 .....	74	37	50.00	36	48.65	7	9.46	0	-----
2 .....	184	138	75.00	132	71.74	25	13.59	6	3.26
3 .....	162	146	90.12	135	83.33	31	19.14	6	3.70
4 .....	153	126	82.35	116	75.82	38	24.84	6	3.92
5 .....	172	155	90.12	141	81.98	47	27.33	11	6.40
6 .....	161	141	87.58	126	78.26	58	36.02	14	8.70
7 to 9 .....	375	337	89.87	270	72.00	202	53.87	33	8.80
10 to 14 .....	495	443	89.49	346	69.90	308	62.22	38	7.68
15 to 30 .....	1,100	980	89.09	671	61.00	741	67.36	104	9.45
31 to 50 .....	955	789	82.62	472	49.42	591	61.89	78	7.96
Over 50 .....	427	361	84.54	205	48.01	277	64.87	48	11.24
Under 15 .....	1,796	1,526	84.97	1,305	72.66	717	39.92	114	6.35
15 and over .....	2,482	2,130	85.82	1,348	54.32	1,609	64.83	228	9.19

Age (years).	<i>Oxyuris</i> .		<i>Tænia</i> .		<i>Hymenolepis</i> .		<i>Strongyloides</i> .		Total infections.	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1 .....	0	-----	0	-----	0	-----	0	-----	4	20.00
1 .....	1	1.35	0	-----	0	-----	0	-----	44	59.46
2 .....	3	1.63	0	-----	0	-----	1	0.54	167	90.76
3 .....	1	0.62	0	-----	0	-----	0	-----	174	107.41
4 .....	4	2.61	1	0.65	1	0.65	0	-----	165	107.84
5 .....	6	3.49	0	-----	0	-----	0	-----	205	113.37
6 .....	4	2.48	1	0.62	0	-----	0	-----	203	126.09
7 to 9 .....	7	1.87	0	-----	2	0.53	1	0.27	515	137.33
10 to 14 .....	6	1.21	2	0.40	0	-----	0	-----	700	141.41
15 to 30 .....	13	1.18	18	1.64	2	0.18	1	0.09	1,550	140.91
31 to 50 .....	13	1.36	23	2.41	0	-----	1	0.10	1,176	123.14
Over 50 .....	6	1.41	14	3.28	0	-----	0	-----	550	128.81
Under 15 .....	32	1.84	4	0.22	3	0.17	2	0.11	2,177	121.21
15 and over .....	32	1.29	55	2.22	2	0.08	2	0.08	3,276	132.40

TABLE VIII.—*Age distribution of infections (males).*

Age (years).	Num- ber exam- ined.	Infected.		<i>Ascaris</i> .		Hookworm.		<i>Trichuris</i> .	
		Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Under 1.....	9	2	22.22	2	22.22	1	11.11	0	-----
1.....	48	21	43.75	20	41.67	4	8.33	0	-----
2.....	97	76	78.35	72	74.23	15	15.46	4	4.12
3.....	81	71	87.65	66	81.48	18	22.22	2	2.47
4.....	84	71	84.52	66	78.57	25	29.76	2	2.38
5.....	86	81	94.19	73	84.88	27	31.40	7	8.14
6.....	86	75	87.21	65	75.58	33	38.37	5	5.81
7 to 9.....	201	180	89.55	139	69.15	122	60.70	17	8.46
10 to 14.....	248	231	93.15	164	66.15	176	70.97	26	10.48
15 to 30.....	586	535	91.30	341	58.19	459	78.33	54	9.21
31 to 50.....	515	446	86.60	239	46.41	374	72.62	39	7.57
Over 50.....	249	210	84.34	102	40.96	178	71.49	23	9.24
Under 15.....	940	808	85.95	667	70.96	421	44.79	63	6.70
15 and over.....	1,350	1,191	88.22	682	50.52	1,011	74.89	116	8.59

Age (years).	<i>Oxyuris</i> .		<i>Tænia</i> .		<i>Hymenolepis</i> .		<i>Strongy- loides</i> .		Total infections.	
	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Under 1.....	0	-----	0	-----	0	-----	0	-----	3	33.33
1.....	0	-----	0	-----	0	-----	0	-----	24	50.00
2.....	3	3.09	0	-----	0	-----	0	-----	94	96.91
3.....	0	-----	0	-----	0	-----	0	-----	86	106.17
4.....	3	3.57	0	-----	0	-----	0	-----	96	114.29
5.....	1	1.16	0	-----	0	-----	0	-----	108	125.58
6.....	2	2.33	1	1.16	0	-----	0	-----	106	123.26
7 to 9.....	2	1.00	0	-----	1	0.50	1	0.50	282	140.30
10 to 14.....	2	0.81	2	0.81	0	-----	0	-----	370	149.19
15 to 30.....	3	0.51	12	2.05	2	0.34	1	0.17	872	148.81
31 to 50.....	5	0.97	14	2.72	0	-----	1	0.19	672	130.49
Over 50.....	2	0.80	6	2.41	0	-----	0	-----	311	124.90
Under 15.....	13	1.38	3	0.32	1	0.11	1	0.11	1,169	124.36
15 and over.....	10	0.74	32	2.37	2	0.15	2	0.15	1,855	137.41

TABLE IX.—Age distribution of infections (females).

Age (years).	Num- ber exam- ined.	Infected.		<i>Ascaris</i> .		Hookworm.		<i>Trichuris</i> .	
		Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Under 1 .....	11	1	9.09	1	9.09	0	-----	0	-----
1 .....	26	16	61.54	16	61.54	3	11.54	0	-----
2 .....	87	62	71.26	60	68.97	10	11.49	2	2.30
3 .....	81	75	92.59	69	85.19	13	16.05	4	4.94
4 .....	69	55	79.71	50	72.46	13	18.84	4	5.80
5 .....	86	74	86.05	68	79.07	20	23.26	4	4.65
6 .....	75	66	88.00	61	81.33	25	33.33	9	12.00
7 to 9 .....	174	157	90.23	131	75.29	80	45.98	16	9.20
10 to 14 .....	247	212	85.83	182	73.68	132	53.44	12	4.86
15 to 30 .....	514	445	86.58	330	64.19	282	54.85	50	9.73
31 to 50 .....	440	343	77.95	233	52.95	217	49.32	37	8.41
Over 50 .....	178	151	84.83	103	57.87	99	55.62	25	14.04
Under 15 .....	856	718	83.88	638	74.53	296	34.58	51	5.96
15 and over .....	1,132	939	82.07	666	58.83	598	52.83	112	9.89

Age (years).	<i>Oxyuris</i> .		<i>Tænia</i> .		<i>Hymenolepis</i> .		<i>Strongy- loides</i> .		Total infections.	
	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.
Under 1 .....	0	-----	0	-----	0	-----	0	-----	1	9.09
1 .....	1	3.85	0	-----	0	-----	0	-----	20	76.92
2 .....	0	-----	0	-----	0	-----	1	1.75	73	83.91
3 .....	1	1.23	0	-----	0	-----	0	-----	87	107.41
4 .....	1	1.45	1	1.45	1	1.45	0	-----	70	101.45
5 .....	5	5.81	0	-----	0	-----	0	-----	97	112.79
6 .....	2	2.67	0	-----	0	-----	0	-----	97	129.33
7 to 9 .....	5	2.87	0	-----	1	0.57	0	-----	233	133.91
10 to 14 .....	4	1.62	0	-----	0	-----	0	-----	330	133.60
15 to 30 .....	10	1.95	6	1.17	0	-----	0	-----	678	131.91
31 to 50 .....	8	1.82	9	2.05	0	-----	0	-----	504	114.55
Over 50 .....	4	2.25	8	4.49	0	-----	0	-----	239	134.27
Under 15 .....	19	2.22	1	0.12	2	0.23	1	0.12	1,008	117.76
15 and over .....	22	2.94	23	2.03	0	-----	0	-----	1,421	125.53

Two infants, one of 3½ months, the other of 9 months, were infected with *Ascaris*; another, of 9 months, with *Ascaris* and hookworm.

The number of infections per 100 persons was greatest in the age group 10 to 14 in the general findings and among the males and among females over 50, namely, 141.41, 149.19 and 134.27, respectively.

The percentages of persons infected with the various parasites are given by years up to the seventh year for the purpose of calling attention to the very high percentage of children, even infants, who harbor intestinal parasites. The results obtained show that infants between 1 and 2 years give an infection of 50 per cent with 59.46 infections per 100 examined. A year later the percentages rise to 75 and 90.76, respectively.

GEOGRAPHICAL DISTRIBUTION.

An attempt was made to study the geographical distribution of the infections among the thirty-three *cabecerias* of San Antonio. The percentages varied as follows:

TABLE X.—*Variation in the percentages of the parasites found at San Antonio according to cabecerias.*

Parasite.	Mini- mum.	Maxi- mum.
	<i>Per cent.</i>	<i>Per cent.</i>
<i>Ascaris</i> .....	31.43	82.44
Hookworm.....	22.06	81.00
<i>Trichuris</i> .....	0.00	63.79
<i>Oxyuris</i> .....	0.00	5.56
<i>Tania</i> .....	0.00	7.55

Since the *cabecerias* vary in population from 58 to about 200, it was to be expected that there would be considerable variation in the percentages of the various parasites found. As a rule the lower percentages were obtained in the smaller *cabecerias*; the higher ones in the larger. This particularly was true in regard to the findings for *Ascaris*. The occurrence of the hookworm seemed to be influenced chiefly by the nature of the sites selected for houses. Where the homes were located upon a rocky soil the infection with hookworms was less than where they were upon the lowlands. For instance, in *cabecerias* 2, 18, and 26, which are built on rocky soil, 23.60, 22.06 and 35.37 per cent were infected against 81.00, 70.59 and 67.09 per cent in *cabecerias* 14, 4 and 13, built on the lowlands. Since women are not found in the fields as often as men, it would be expected that a greater percentage of men would be infected if the infection took place in the fields (lowlands). This was found to be the case in the whole series (74.89 per cent against 52.83 per cent) and in the representative *cabecerias* under discussion as shown below.



TABLE XI.—*Hookworm findings in men and women in selected cabecerias.*

Number of cabe- ceria.	Group A. Located on rocky soil.						
	Men.			Women.			
	Exam- ined.	Positive.	Per cent.	Exam- ined.	Positive.	Per cent.	
2	37	15	40.54	42	12	28.57	
18	9	9	47.37	19	4	21.05	
26	26	13	50.00	25	8	32.00	
	Group B. Located on lowlands.						
	4	25	24	96.00	29	18	62.07
	13	26	20	76.92	25	14	56.00
	14	40	37	92.50	28	23	82.14

The geographical distribution of infections with *Trichuris* was influenced by the 58 Visayans, 63.79 per cent of whom were infected with this parasite, and association with people in Ilagan *Central*. The Visayans had been at the hacienda about one year and undoubtedly carried the parasites into the valley with them. The whipworm was found more frequently among the persons living in *cabecerias* near them, than among those in other parts of the hacienda. The people who lived nearer Ilagan *Central* were more frequently infected with this parasite than those farther away, excepting the Visayans and their neighbors. The infections probably took place while the individuals were visiting in the town. These opinions are supported by the fact that Maluno, which has no Visayans and which is located at quite a distance from Ilagan *Central*, so that visiting is inconvenient, had fewer with *Trichuris* than had San Antonio.

The majority of the infections with *Tænia* occurred in *cabecerias* which are located near the mountains where it is the custom to hunt occasionally. During these hunting trips raw pork or deer meat is sometimes eaten.

#### MEDICAL SIGNIFICANCE.

While the investigation had, as one of its objects, the determination of the medical significance of the infections found, particularly those with the hookworm, its chief aim was to obtain statistics relative to the incidence of the various parasites. The great majority of cases were seen only once so that it was impracticable to study them clinically. Nothing can be said definitely regarding the influence of intestinal parasites at the

haciendas, but nevertheless, general impressions as to the physical condition of the inhabitants were received. As a class, the people are anæmic and they have very little ambition. Many of the children present marked evidence of ascariasis. It was attempted repeatedly to select cases of infection with the hookworm before the microscopic examinations were made, but only unsatisfactory results were obtained.

It was not difficult to secure a history of symptoms which are frequently present in intestinal helminthiasis, such as nausea, vomiting, pain in various parts of the abdomen, constipation, diarrhœa, headache, dizziness, and restlessness, but it can not be stated that these symptoms were caused by the parasitic infections. Many factors are acting upon these people to lower their vitality and give rise to the symptoms mentioned. Climate, early marriage, rapid child bearing, poor food, excessive smoking, habitual use of alcoholics, and tuberculosis, all have their influence as well as the parasites. To determine the proportion of the symptoms due to helminthiasis would be a difficult problem, the solution of which would require most careful study extended over a considerable period of time.

The important question of the significance of hookworm infections among the Filipinos remains unanswered. A few years ago infections with this parasite were considered to be of importance, but during the past two years, there has been a growing tendency to attach less and less significance to them until now some believe them to be so mild that their influence is practically *nil*, or that the Filipinos enjoy a degree of immunity to the effects of the parasite. Such a change in opinion is neither a strange occurrence, nor one peculiar to the Philippine Islands. Beliefs regarding the significance of hookworm infections in the United States have varied. Too much importance was attributed to mild infections a few years ago, whereas, in my opinion there is an inclination to attach too little to them at present. It is the consensus of opinion among those who have worked with intestinal parasitism in the Islands that marked cases of the disease are rare among Filipinos. On the other hand, it has not been proved that the infections are so mild as to be of no importance from an economic point of view, or that of health. That intestinal parasitism has an effect upon mortality and morbid conditions in the Philippines is evidenced by the results obtained at Bilibid prison upon the institution of a routine examination and a routine treatment against the parasites. The Director of Health reports that a few years ago, when the Bureau of Health began its work at the prison, the annual death rate was 238 per 1,000. In response to the institution of sundry hygienic measures, the mortality fell to 75 per 1,000, and it seemed impossible to decrease the death rate beyond this figure. At this time the routine examination of the fæces for evidences of intestinal parasitism and the routine treatment of infected cases was begun, with the result that the

death rate fell to 13.5 per 1,000 per annum. The routine work has been continued and the death rate has remained low. In addition to this general finding, the Director of Health tells me that the fall in the death rate occurred in brigade after brigade of the prison as the examination and treatment progressed from one to another; this is more convincing than the general findings that the fall in the mortality was due to the expulsion of animal parasites from the intestinal tract. Prior to the inauguration of this work deaths had rarely been attributed to intestinal parasites excepting *Amæba coli*. This is in keeping with the generally accepted opinion among medical zoölogists that the chief influence of helminthiasis is so to lower the vitality of the host that he is more susceptible to other diseases.

The statistical results of the examinations at Bilibid Prison were reported by Garrison. (Table III.) It is noteworthy that the hookworm ranked second in point of frequency. If the treatment for intestinal parasitism was an important factor in the remarkable decrease in the mortality at this prison, it is impossible to believe that the hookworm did no injury, as compared to that done by *Ascaris*, *Trichuris* and the other parasites present.

The fact should not be overlooked that Garrison found 142 infections with intestinal worms per 100 persons examined. Considerable work at Bilibid has convinced me that the hookworm is almost invariably associated with one or two, and sometimes more parasites. The results obtained at the prison must not be attributed to the expulsion of hookworms, but to the cleaning of the intestinal tract of parasites in general. It is quite possible that the hookworm occurring alone is of little significance and the same may be true of *Ascaris* and *Trichuris*, etc., but that when several infections occur in one individual, they are of considerable importance. I am persuaded that were 10 (instead of one) cover-slip preparations of the fæces of each case examined at Bilibid, fully 98 per cent of Filipinos entering the prison for the first time would be found to harbor one or more intestinal parasites; and that there would be very few single infections.

It seems incredible that the remarkable fall in the death rate at Bilibid Prison was alone due to treatment for intestinal parasites. The general hygienic conditions at the prison have been improved year after year since the Bureau of Health was given control of the health problems of the jail. In my opinion, some of the sanitary measures introduced contributed to the low death rate during the year in which the routine treatment for intestinal parasitism was inaugurated. On the other hand, the immediate fall in the mortality upon the institution of the routine treatment is quite too remarkable to be considered as a mere coincidence. The writer believes that the results obtained prove that intestinal parasitism is of no inconsiderable significance among the Filipinos.

Since parasites apparently contributed to the death rate at Bilibid Prison, it is permissible to believe that they are to be reckoned with in considering the morbidity; that is, the problem of intestinal parasitism is not only of medical but, also, of economic importance.

Confronted with the results obtained at Bilibid Prison and with those of the statistical studies of over 19,000 people in the Islands, approximately 85 per cent of whom, as the result of a meager examination were found to harbor one or more parasites, the problem of the proper disposal of human excreta is brought vividly to our attention. The fact that cholera, the various dysenteries, and other diseases would markedly be influenced by a proper disposal of the excreta does not subtract from the importance of the problem.

#### ACKNOWLEDGMENTS.

I was in the Cagayan Valley at a time when the people were very busy with their crops. The two haciendas are broken up into small *cabecerias*, and the tenants are provided with medical advice and treatment free of charge; thus my endeavors to make this study must have failed but for the coöperation of Señores Orros and Mesa, *administradores* of San Antonio and Maluno, respectively. I wish to acknowledge my indebtedness to them and their assistants for many courtesies.

Mr. Manuel Ramirez and Mr. Rafael Santos, fourth-year students in the College of Medicine and Surgery, University of the Philippines, rendered me valuable assistance in the examinations, and I wish to express my thanks to them also for their thorough, painstaking work.

## A NOTE UPON ANTHRAX IN THE PHILIPPINE ISLANDS.

---

By W. H. BOYNTON.<sup>1</sup>

---

The existence of anthrax in the Philippines appears to have attracted very little attention. The only reference to it in print is by McMullen,<sup>2</sup> who was sent to the pueblo of Tagudin, Province of Ilocos Sur, in January, 1904, to investigate reports of a disease among animals the outbreaks of which antedated the American occupation. The disease occurred each year at the end of the rainy season and was most virulent at the onset of the outbreaks, killing animals in from two hours to three days after the first appearance of symptoms. Microscopic examinations of the blood from the viscera of animals dead of this infection revealed anthrax bacteria. Cultures were made in the Government laboratories in Manila.

In April, 1904, Doctor Lusk, veterinarian of the Second Cavalry, United States Army, reported the death of two mules from anthrax at Camp Wallace, La Union. These animals were of a pack train which plied between Camp Wallace and Benguet. The infection was supposed to have been contracted along the trail.

In addition to these observations, the correspondence files of the Bureau of Agriculture contain a few references to anthrax. The places mentioned are the townships of Bauco and Cayan, in the subprovince of Lepanto, Mountain Province; and Sual, Pangasinan. The existence of anthrax in Lepanto-Bontoc was questioned by a second veterinarian who investigated the matter. No evidence is at hand to show that any diagnosis in these outbreaks was confirmed by cultures. The records also show that three shipments of cattle from Hongkong were quarantined for anthrax.

### ANTHRAX IN TAYTAY, RIZAL.

Dr. C. G. Thompson, in charge of the serum laboratory at Alabang, on the 14th of August, 1910, called the writer's attention to a smear preparation of blood made by Mr. Cattell, a live-stock inspector for the Bureau of Agriculture. This preparation was taken from a carabao

<sup>1</sup>Pathologist, Bureau of Agriculture, Manila, P. I.

<sup>2</sup>A Preliminary Report on the Presence of Anthrax in the Philippine Islands. *Am. Vet. Rev.* (1904-1905), 28, 935.

which had died very suddenly in the vicinity of Taytay. Mr. Cattell stated that he made the smear immediately after the death of the animal. The staining material at hand was not of the best kind for distinguishing anthrax. However, upon microscopic examination, there was observed a large number of rather long, rod-shaped organisms with square-cut ends, some of them in chains, and others single, many being surrounded by what appeared to be capsules. It hardly seemed probable that these bacteria were putrefactive organisms, since the preparation was taken from the animal soon after death, but to be sure of the fact several guinea pigs were sent to Taytay, and instructions were given to the effect that if any animals there died in a similar manner a guinea pig should be inoculated with some of the blood, smear preparations made, a piece of the ear of the dead animal cut off, and both ear and smear preparations sent to the writer's laboratory at the Bureau of Science in Manila.

CASE I, *number 17*.—Carabao owned by Juan Villanueva, Santa Ana, Taytay, Rizal; died August 30, 1910. One guinea pig inoculated at 2.40 p. m., August 30, with blood taken from this animal after death; two smear preparations and a piece of the ear of the dead carabao were received on the morning of August 31.

The smear preparations were stained with an aqueous solution of methylene blue, recommended by M'Fadyean.<sup>3</sup> A large number of rod-shaped organisms with square-cut ends, occurring singly, in pairs and in chains, were present. Practically every organism was surrounded by an amorphous, violet or reddish-purple granular material. M'Fadyean states that he has never found this reaction in animals dead from diseases other than anthrax.

Smear preparations were made from blood procured from the ear. These smears were stained in a similar manner, and similar results were obtained. Agar cultures were made from blood obtained from the ear.

*September 1*: Guinea pig was found dead in the laboratory in the morning. Smear preparations made from the spleen, liver, and heart blood showed the presence of anthrax bacteria in stained preparations. Frozen sections made of the kidney, stained with carbol-fuchsin, showed the presence of anthrax bacteria in the capillaries between the tubules and in the glomeruli. Agar cultures were made from the spleen, liver, and heart blood. Agar culture made from the ear showed almost pure culture of anthrax bacteria characterized by the ground-glass appearance along the edge of the colonies, and showed, under the low power of microscope, long flexible filaments combining to form thread-like bundles.

*September 2*: Agar culture made from spleen, liver, and heart blood showed pure cultures of anthrax. An emulsion of some of the cultures obtained from the spleen was made in sterile water, and 1 cubic centimeter of this was injected subcutaneously into a guinea pig.

*September 3*: Guinea pig was found dead in the morning. Smear preparations from the spleen, liver, and heart blood showed the presence of large numbers of anthrax bacteria. Agar cultures were made from these organs.

*September 4*: Agar cultures made from spleen, liver, and heart blood showed pure cultures of anthrax bacteria.

Juan Villanueva owns another carabao, which, up to September 14, appeared

<sup>3</sup> A Peculiar Staining Reaction of the Blood of Animals Dead of Anthrax. *Journ. Comp. Path. & Therap.* (1903), **16**, 35.

to be in perfect health. He has not had any animals die suddenly before this one, except in 1901, when, he says, a carabao died with rinderpest. The animal which died of anthrax was purchased by him from dealers from Binangonan Malayo, Tayabas Province, in December, 1909. It was kept every day in a pasture called Libis, with many other carabaos. This pasture is situated between Taytay and Laguna de Bay.

CASE II, number 19.—Carabao owned by Saturnino Morales, Santa Ana, Taytay, Province of Rizal, died September 1, 1910. Guinea pig was inoculated on September 1, at 10.55 a. m., with blood from dead carabao. One smear preparation of blood and piece of animal's ear were received at the laboratory on the afternoon of September 1. Smear preparation of the blood, stained with aqueous methylene blue showed the presence of a large number of anthrax organisms giving M'Fadyean's reaction.

Smear preparations from ear of carabao stained with aqueous methylene blue showed the presence of large numbers of anthrax bacteria giving the same reaction. Agar cultures were made from blood of carabao's ear.

September 2: Agar cultures showed characteristic anthrax colonies, and cover-glass preparations showed the presence of anthrax bacteria.

Guinea pig died 11.30 a. m. Anthrax bacteria were found present in smears from spleen, liver, and heart blood, giving characteristic reaction to aqueous methylene blue. Frozen section of kidney stained with carbol-fuchsin showed anthrax bacteria present in capillaries of convoluting tubules, collecting tubules, and glomeruli.

Agar cultures were made from blood of spleen, liver, and heart.

September 3: Agar cultures made on September 2 showed pure culture of anthrax bacteria from spleen, liver, and heart blood.

This carabao was the only one owned by Saturnino Morales at the time of its death and when very young was brought from Antipolo. At the time of its death it was pastured every day along with a large number of other carabaos in a pasture place called Mahabang Sapa, which is separated from Libis by a shallow river.

CASE III, number 23.—Carabao owned by Victor Santos, barrio of San Juan, Taytay, Rizal, died September 8, 1910. Guinea pig was inoculated 8.35 a. m., and ear of carabao was received in laboratory about noon on the 8th.

Smears of blood from ear stained with aqueous methylene blue showed presence of anthrax organisms and gave M'Fadyean's reaction. Agar cultures were made from blood of ear.

September 9: Guinea pig was found dead and very much distended, showing that it probably had died on the evening of the 8th. Smear preparations made from the spleen, liver, and heart blood, stained with aqueous methylene blue, showed an enormous number of rod-shaped organisms. Some of them resembled anthrax, giving the characteristic reaction, while the others had the appearance of putrefactive organisms. Agar cultures were made from blood of spleen, liver, and heart.

Agar culture from ear gave practically pure culture of anthrax.

September 10: Agar cultures from spleen, liver, and heart blood showed mixed cultures; a few anthrax colonies were distinguished. Cover-glass preparations from these showed anthrax bacteria.

Victor Santos does not own any other carabao. The one which died was bought in Binangonan Malayo about two years ago. It was pastured every day along with many other carabaos in the pasture called Libis. Several years before a carabao owned by him died, but the nature of the death could not be ascertained.

CASE IV, *number 25*—Carabao owned by Pedro Banals, San Gaibro, Taytay, Rizal, died September 13, 1910. The ear of the carabao was received in the laboratory early in the morning of the 14th. In smear preparations from the blood of the ear, stained with aqueous methylene blue, no rod-shaped organisms could be found. The only organisms seen were a very few micrococci. Agar cultures were made of blood from the ear.

*September 15:* Agar cultures showed no anthrax colonies, there being a few scattered colonies which resembled *Micrococcus pyogenes aureus*. Cover-glass preparations from several colonies stained with aqueous methylene blue<sup>1</sup> showed the presence of a micrococcus. As far as can be decided from smear preparations and cultures, it would appear that this animal did not die of anthrax.

This man owns three more carabaos. These and the dead one were pastured every day in a pasture called Mapandon, with many other carabaos. He bought the carabao which died in San Mateo, Rizal, about three months before.

CASE V, *number 32*.—Carabao owned by Rufino del Rosario, Mapondon, Taytay, Province of Rizal; died on the evening of September 28, 1910.

The ear of the carabao received in the laboratory early in the morning of the 29th. Smear of blood from the ear stained with aqueous methylene blue showed presence of anthrax organisms giving M'Fadyean's reaction. Agar cultures were made from blood of ear.

*September 30:* Agar cultures from ear gave practically pure cultures of anthrax.

This man owns five more carabaos, which, with the one that died, were pastured every day with many other carabaos, in Mapandan, a pasture ground situated on the opposite side of the town from Libis.

CASE VI, *number 33*.—Carabao owned by Mariano de los Reyes, San Isidro, Taytay, Rizal, died on the morning of September 29, 1910.

The ear of the carabao was received in the laboratory on the morning of the 30th. Smears of blood from the ear, stained with aqueous methylene blue, showed presence of anthrax organisms giving M'Fadyean's reaction. Agar cultures were made from blood of ear.

*October 1:* Agar cultures from ear gave practically pure cultures of anthrax.

This man owns two more carabaos. These and the dead one were pastured every day with many other carabaos in a pasture called Lambac, a subdivision of Libis. He had owned this carabao several years.

CASE VII, *number 39*.—Carabao owned by Lazaro del Valle, barrio of San Isidro, Taytay, Rizal, died October 27, 1910.

The ear and two blood smears from the carabao were received in the laboratory on the afternoon of the 27th. Blood smear stained with aqueous methylene blue showed presence of anthrax organisms giving M'Fadyean's reaction. Agar cultures were made from blood of ear.

*October 28:* Agar cultures showed practically pure culture of anthrax.

This carabao was pastured on the 14th and 15th of October in Libis, but from the 15th of October to the time of its death the carabao was pastured in the fields of the barrio of San Isidro.

#### CONCLUSION.

1. From the results derived from the cultures, staining reaction, and animal inoculations, it is evident that anthrax exists in the vicinity of Taytay.



2. Since the animals, which were proved to have died of anthrax, were pastured in Libis, Mahabang Sapa, Mapandan, Lambac, and San Isidro, the infection is shown to be widely disseminated around the town of Taytay.

3. As it is almost impossible to procure definite information as to the number of animals and the manner in which they died in these places, one can not state whether the infection is recent or of long standing in this vicinity. The general opinion of the veterinarians is that it is of long standing, but has not been recognized as anthrax prior to this time.



## REVIEW.

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**Primer of Sanitation for the Tropics.** By John Woodside Ritchie and Margaret Anna Purcell. Cloth. Pp. x + 182. Illustrated by 94 figures. Price \$0.60. Yonkers-on-Hudson: World Book Co., 1910.

This little book undoubtedly is one of the best of its kind that has come to our notice, and could well be adopted by the public schools of the United States with certain changes to suit the different conditions there. By following its teachings children can soon learn the simple principles of cleanliness and how to avoid disease.

The book treats of the causes of infectious diseases, what germs are, how they get into the body, how the body fights them, and how to avoid them. The principal diseases of the Tropics, such as cholera, dysentery, malaria, tetanus, tuberculosis, etc., are discussed in a language that any child can understand, and there is a sufficient repetition of the axioms governing a healthy life to impress the mind with their importance. In fact we can recommend the perusal of this valuable little work to adults as well as to children.

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## INVESTIGATION ON THE ACTION OF THE TROPICAL SUN ON MEN AND ANIMALS.

By HANS ARON.

*(From the Physiological Laboratory, College of Medicine and Surgery, University  
of the Philippines, Manila, P. I.)*

The meteorologic conditions which surround us, such as temperature, humidity, barometric pressure and the movements in the atmosphere, all of which, to a great extent, are controlled by the radiation of the sun, are included under the designation of climate. Each of these factors of environment has its characteristic influence upon the life functions of living organisms. We can, on the one hand, study the influence of differing temperatures, humidities, and movements and pressures of the air on men and animals in modern respiration calorimeters without the need of conducting the work in a particular climate. Rubner,<sup>1</sup> especially, has carried on such work. But, on the other hand, the action of the sun of a given latitude can not be reproduced artificially.

The radiant energy of the sun which reaches the atmosphere is in part absorbed while passing through the latter, and this absorption, other conditions being equal, should be smaller the less deep the absorbing layer. If conditions, such as layers of the atmosphere of unequal density which would tend to refract the rays, do not intervene, and again, if all other conditions are equal, the absorption is smallest during the vertical incidence of the rays; that is, when the sun is in the zenith.

<sup>1</sup> *Arch. f. Hyg.* (1894), 20, 309-312, 345-364, 365-371; (1895), 23, 87, 13-43; (1900), 38, 120-159. *Die Gesetze des Energieverbrauches bei der Ernährung*, Leipzig-Wien (1902).

Because of the more nearly vertical incidence of the sun's rays in the Tropics, a greater proportion reaches the earth and with a greater intensity on a given area than in the northern and southern latitudes. Of course, in granting this, such phenomena as cloud formation are excluded.

The tropical sunlight, in so far as the violet and ultra-violet end of the spectrum is concerned, has been studied extensively in the past few years in the Bureau of Science in Manila by Freer,<sup>2</sup> Gibbs,<sup>3</sup> and Bacon,<sup>4</sup> and the effects produced by this portion of the sunlight have been and are being compared with those obtainable by observers using the same means of measurement in other latitudes. These investigations up to the present have shown that the spectrum of the sun's rays does not extend much, if any, farther into the ultra-violet in Manila than in northern climates. Observations carried on daily during the year on the decomposition of a solution of oxalic acid under the influence of uranyl acetate as a catalyzer<sup>5</sup> have shown as great variations between individual days, even of the same apparent brightness, and some decomposition even on cloudy and rainy days; however, with a general tendency toward maximum decomposition when the sun is nearest the zenith and of minimum under opposite conditions. The comparative measurements in other countries are not as yet available to any extent, with one exception. Bacon showed that the decomposition in Manila in July was from five to twenty times greater than in Chicago in June.

The work with the ultra-violet spectrum was of interest not only because it is necessary thoroughly to consider these rays in a study of tropical sunlight, but also because of the number of authors,<sup>6</sup> especially in modern times, who are inclined to the belief that the action of the tropical sun on the human organism is to be attributed to the influence of the rays of shorter wave length. As a result of this belief a special underwear, which by its color should be impermeable to the ultra-violet rays, has recently been recommended for use in the Tropics.

An extensive investigation of the relation of the color of underwear to the health of men in this climate was made by Phalen and Nichols<sup>7</sup>

<sup>2</sup> *This Journal*, Sec. B (1910), 5, 1.

<sup>3</sup> *Ibid.*, Sec. A (1909), 4, 133; (1910), 5, 9 and 419.

<sup>4</sup> *Ibid.* (1910), 5, 267.

<sup>5</sup> The solution of oxalic acid uranyl acetate is only acted upon by the ultra-violet end of the spectrum. The results of this work will be published later from the Bureau of Science.

<sup>6</sup> Woodruff, C. E., *The Effects of Tropical Light on White Men*. New York and London, (1905); Duncan, *Journ. Roy. Army Med. Corps* (1908), 11, 71; Simpson, *Ibid.*, 441-449; Gihon, *Twentieth Century Practice of Medicine*, New York (1895), 3, 253-285.

<sup>7</sup> *This Journal*, Sec. B (1911), 6, 525.

on 1,000 American soldiers in the Philippines. The results, as to the advantage of orange-red, were negative. This fact, when considered in connection with a number of observations which I have made during my stay in the Tropics, convinced me that the rays of the tropical sun having greater wave length, that is, those in the red and ultra-red end of the spectrum, play the most important rôle in producing the untoward effects generally attributed to tropical sunlight.

In making this statement it must be understood that it refers to organisms having the capability of regulating the body heat, and not to those low in the scale, such as bacteria or protozoa, for it has been shown repeatedly<sup>8</sup> that in the case of the latter ultra-violet rays exert a most destructive action, heat coming into consideration only in so far as such organisms are not able to live when the temperature is above a certain point. Plants also, the normal life action of which depends on the chlorophyll, of course are markedly affected by the ultra-violet as well as by the other end of the spectrum.

In order correctly to interpret the experiments given in subsequent portions of this paper, it will be necessary briefly to review the physiologic processes concerned in heat regulation in the bodies of mammalia.

The body possesses the capability not only of regulating its heat production from the combustion of foodstuffs (chemical heat regulation), but also its loss of heat from convection, radiation and water evaporation (physical heat regulation). Normally, the thermal effects of the surroundings are compensated either by a suitable transference of heat to the surroundings, or by the conservation or production of heat within the body, so that the body temperature within narrow limits remains practically the same. However, there are limits to the power of regulation. If the body is heated too intensively or the loss of heat is inhibited, the latter will accumulate and the body temperature rise.

The higher the temperature of the surroundings, the less will be the loss of heat by conduction or radiation, and if this temperature exceeds that of the body, no heat can be lost in this way, but on the contrary the balance is changed, and the energy lost to the body would now be accumulated in it were it not for the loss occasioned by the evaporation of water from the lungs and the surface of the body.

High air temperatures alone do not change the body temperature as long as the latter can be regulated by the loss of sufficient heat through water evaporation.<sup>9</sup> Therefore, a man can withstand temperatures even of 129° for a considerable time if the air is comparatively free from water vapor. On the other hand, if the relative humidity is high and,

<sup>8</sup> *Loc. cit.*

<sup>9</sup> Hill, Leonard, Recent Advances in Physiology and Biochemistry, London, (1908), 256-274.

therefore, the evaporation of water from the body lessened, the loss of heat is inhibited.<sup>10</sup> It will be recalled that in many localities in America or Africa the thermometer in summer often is much higher than it is in the Tropics, yet the heat by no means produces the same effect. The humidity in the Tropics is always comparatively high, because the air for considerable periods of time is nearly saturated with water vapor. It might be stated that it is not regions of high air temperatures, but those having a high relative humidity which produce especially untoward effects by reason of their climate.<sup>11</sup> However, if the air is in motion, even if it is very humid and hot, increased water evaporation and conduction bring about a great loss of heat. This fact is of great importance in the Tropics. The fresh winds prevalent here render the climate of Manila in the months of May to August much more tolerable to human beings than is the case in certain parts of the Chinese coast or even on the Atlantic seaboard which lie considerably farther to the north.

Generally speaking, the majority of people living in the Tropics are on the coastal or intermontane plains, where the climatic conditions are nearly alike throughout the year. The high air temperatures and high relative humidity are maintained so that conditions retarding the loss of body heat are practically continuous, in distinction from those regions where, despite the fact that at certain times the heat and relative humidity are high, nevertheless the average for the year is low. However, the body temperature of man and probably also of animals, in spite of this fact, normally does not exceed the physiologic limits. This has been shown by a large number of careful measurements of body temperatures of white and colored men in the Tropics, and of the same people in the Tropics and in temperate climates. Variations, when they have been observed, are doubtless not greater than the daily ones encountered in other climates.

Finally, the radiation from the sun is obviously an important factor. Any object exposed to the sun's rays absorbs a portion of them. The majority of substances, and among them is included the animal body, have a much higher coefficient of absorption for heat than has the air, and therefore they become hotter in the sun than does the surrounding air. This effect of the heat radiated from the sun, while generally most intense in the Tropics, is present in all latitudes. Rubner, Cramer,<sup>12</sup> and Wolpert<sup>12</sup> have studied the results of insolation in temperate climates. According to their experience we can calculate approximately

<sup>10</sup> Haldane, *Journ. Hyg.*, Cambridge (1905), 5, 494.

<sup>11</sup> Of course it must be recalled that in the Tropics, where the relative humidity is high, the sun is often obscured by clouds.

<sup>12</sup> *Arch. f. Hyg.* (1894), 20, 313-344; (1892), 33, 206-228; (1902), 44, 322-338.

the temperature which corresponds to the thermic effect of the sun by adding half the number of degrees difference between the register of the black-bulb thermometer in the sun and the shade thermometer to the shade temperature. Applying this calculation to the conditions in the direct sunlight at Manila or other tropical place, for instance, Colombo, we find that this temperature is considerably above the one normal for the body.

The pyrliometer devised by Angstrom<sup>13</sup> alone seems capable of measuring exactly the caloric value of the radiation of the sun. This instrument has been adopted by an international meteorologic conference in Innsbruck. Measurements with it have been made in other parts of the world, but as yet no work has been done with it in the Tropics. The Rev. José Algue, S. J., Director of the Weather Bureau in Manila, has begun such investigations in connection with our experiments. However, an important part of his apparatus was broken, so that after repairs on it had been completed here, we could obtain only relative values for the different days. A new apparatus has been ordered and the figures after its arrival will be recalculated into absolute values.<sup>14</sup>

Therefore, we will shortly be in a position to furnish exact values for Manila and other places in the Philippines obtained by the pyrliometer. It seems urgent that comparative studies in other parts of the world, especially tropical and subtropical regions, be made with the standard instrument of Angstrom. P. Schmidt estimates the heat effect of the tropical sun as being equal to 2 gram calories per square centimeter per minute.

I have found in the literature only a few observations concerning the action of the tropical sun on animals.

Scaghosi<sup>15</sup> exposed rabbits to the sun in Sicily. Their temperatures rose markedly, and upon continuing the experiment for a sufficient length of time, the animals died. Recovery took place if the direct insolation was stopped in sufficient time. Castellani and Chalmers<sup>16</sup> report some experiments which they performed in Colombo. They exposed rabbits with their heads shaved to the noon sun. The animals died in about sixty-seven minutes with all the symptoms and post-mortem appearances of sunstroke. Another rabbit, similarly treated, but protected by a red glass, lived. These authors concluded that sunlight can bring about "(1) sudden death, (2) congestion of the meninges of the brain. The ultra-violet rays seemed to have no effect and it would appear as if the active rays were in the visible violet." Of course the red glass also absorbed a very large proportion of the heat rays.

<sup>13</sup> *Astrophys. Journ.* (1899), 9, 332.

<sup>14</sup> My thanks are due to the Rev. José Algue and to the Rev. Juan Comellas for the valuable assistance they have rendered, not only by the loan of apparatus and by conducting measurements, but also for advice on meteorologic subjects.

<sup>15</sup> Castellani and Chalmers, *Manual of Tropical Medicine*, London (1910), 86.

<sup>16</sup> *Ibid.*

Schilling<sup>17</sup> mentions a few experiments on rabbits: A thermometer under the skin of a white rabbit in the shade showed 38°.4. The animal was transferred into the sun (air temperature about 26°, black-bulb thermometer 46°.7). After half an hour the thermometer under the skin showed 40°.4. The skin was shaved, whereupon after half an hour the thermometer rose to 41°.5. The shaved skin was covered with a piece of black cotton cloth and within twenty-five minutes the temperature rose to 42°.8, the black cloth was removed and the thermometer fell to 39°.6, finally the same place on the skin was blackened with carbon, and within ten minutes the temperature rose to 42°.4. P. Schmidt<sup>18</sup> also exposed rabbits to the sun, but in a temperate climate, and observed in a white rabbit that the temperature *in ano* rose from 38°.5 to 39°.5 and from 38°.5 to 40°.2 in a black rabbit. The increase in temperature during one hour was only 0°.3 if the neck alone was exposed to the sun.

#### EXPERIMENTAL.

If the body of a dead dog or rabbit is placed in the sun of Manila, the temperature of the outer portion of the body, measured by introducing a thermometer under the skin, rapidly rises to 45° and more, thus exceeding the temperature of the surroundings. The absorbed heat will finally also warm up the deeper parts of the body, and therefore a thermometer placed in the rectum will rise. The figures obtained by experiments on dead animals are shown in Table I.

TABLE I.—*Rise in temperature of the bodies of dead animals exposed to the sun in Manila.*

Date.	Remarks.	Time.	Temperature.		Black-bulb thermometer.	Mercury thermometer in sun.
			In ano.	Under the skin.		
1910.			°C.	°C.		°C.
Sept. 22	Dead rabbit placed on a board in sun at 8 a. m.	10.00 a. m.	-----	43.0	53°.1 at 11 a. m.	-----
		11.00 a. m.	-----	46.2	-----	-----
Oct. 5	Brown dog, hung in sun on a vertical stick at 2 p. m.	2.30 p. m.	36.0	40.0	51°.4 at 2 p. m.	32.0
		3.00 p. m.	36.1	45.3	-----	32.1
		3.30 p. m.	36.3	47.0	-----	32.1
		4.00 p. m.	37.7	47.2	-----	30.7

Of course, the body of a living animal exposed to the sun absorbs heat just as does that of a dead one, and so its temperature would rise in a similar manner were it not able to lose heat more rapidly by reason of its capacity for physical heat regulation.

A dog placed in the sun very soon exhibits the symptoms known as heat-hyperpnœa. Its respiration becomes quicker and forced, the tongue hangs from the mouth and saliva increases and drops from it. As

<sup>17</sup> *Arch. f. Schiffs.-u. Trop.-Hyg.* (1909), 13, 1.

<sup>18</sup> *Arch. f. Hyg.* (1903), 47, 262–290; (1908), 65, 17–31; (1909), 65, 1–20; *Arch. f. Schiffs.-u. Trop.-Hyg.* (1901), 5, 207–233; 245–271.

dogs have no sweat glands, the evaporation of water, which in men is brought about by the secretion of sweat, is replaced in these animals by increased evaporation from the surfaces of the lungs, mouth, and especially the tongue.

However, in spite of the increased water evaporation, the body temperature measured *in ano* of the dog in the direct rays of the sun for several hours may rise  $0^{\circ}.5$  to  $1^{\circ}$ . If the temperature is measured by inserting a thermometer or a thermopile into the subcutaneous tissues through a small incision of the skin, the subcutaneous temperature is found to be above  $40^{\circ}$ .

In a number of experiments, two comparable rabbits in each instance were kept side by side a few paces apart, one in the shade of a house or a wooden wall, the other exposed to the sun. The animals in the sun died in from one to three hours, the temperature *in ano* rising to febrile heights, the subcutaneous temperature in the sun increasing considerably above that simultaneously taken *in recto*. The animals in the shade behaved normally, their temperatures increasing but slightly.

TABLE II.—*Temperature, subcutaneous and rectal, of rabbits in the sun and shade.*

Date.	Remarks.	Time.	Temperature of rabbit in sun.		Temperature of rabbit in shade.		Temperature air in shade.	Black-bulb thermometer.
			Subcutaneous.	Rectal.	Subcutaneous.	Rectal.		
1910. Oct. 12	Two white rabbits. In animal house. Exposed 8 a. m.	7.55 a. m.	$36.8$	$37.5$	$36.4$	$37.6$	-----	$42^{\circ}$ at 11 a. m.
		8.15 a. m.	$37.8$	$37.8$	$36.5$	$37.4$	$27.4$	
		8.30 a. m.	$38.3$	$37.8$	$36.5$	$37.5$	$27.5$	
		8.45 a. m.	$39.1$	$37.8$	$36.8$	$37.4$	$29.6$	
		9.00 a. m.	$39.2$	$38.8$	$36.8$	$37.5$	$30.0$	
		9.15 a. m.	$39.8$	$39.0$	$36.8$	$37.6$	$29.4$	
		9.30 a. m.	$40.8$	$39.2$	$37.9$	$37.9$	$30.7$	
		9.45 a. m.	$41.9$	$40.6$	$38.0$	$38.0$	$30.5$	
		9.50 a. m.	{ Experiment discontinued, animals taken in.					$54^{\circ}$ at 11 a. m.
Oct. 18	Two brown rabbits. In animal house. Exposed 8.25 a. m.	8.20 a. m.	$36.5$	$38.0$	$36.4$	$37.7$	-----	
		8.50 a. m.	$40.7$	$39.0$	$36.5$	$37.5$	-----	
		9.20 a. m.	$44.5$	$42.3$	$37.6$	$37.8$	-----	
		9.50 a. m.	Animal dead.		$37.9$	$38.1$	-----	

Under the climatic conditions surrounding our experiments the number of calories lost depends mainly on the amount of water evaporated in a given time. A dog, by its peculiar hyperpnoea can evaporate relatively more water, and thus lose more heat than the rabbit. However, if we tracheotomize the animal this evaporation is inhibited. The expired air escapes through the tracheal cannula, so that the water vapor carried with the current can not reach the surface of the tongue, and therefore there is but a limited surface from which it can be evaporated.

In the shade, or inside of a room, a tracheotomized dog, while limited

in its power of losing heat, shows a body temperature not above normal, but if such an animal is brought into the direct rays of the sun, the hyperpnoea appears just as with a normal dog but without so great an evaporation of water. Under these conditions the rectal temperature rises to febrile heights. If the experiment is continued for a longer time, the animal finally falls and dies, the respiration having markedly increased, the pulse greatly quickened, cyanosis of the mucous membrane having set in, saliva dropping from the mouth and secretion even having set in from the mucous membrane of the nose. In fact, the animal shows all the symptoms of heat stroke. I have several times interrupted the experiment before this last stage was reached. Then, if the temperature was not too high, it was possible to save the animals. The animals died in two experiments; one, after a few minutes, the other after several hours in spite of careful treatment with cool water. During this time the animal exhibited signs of disturbed orientation; it ran restlessly around, knocked its head against the wall, fell and jumped up again. These severe disturbances of the nervous system correspond to certain observations made during heat stroke in man. The conditions described above are made clear by Table III.

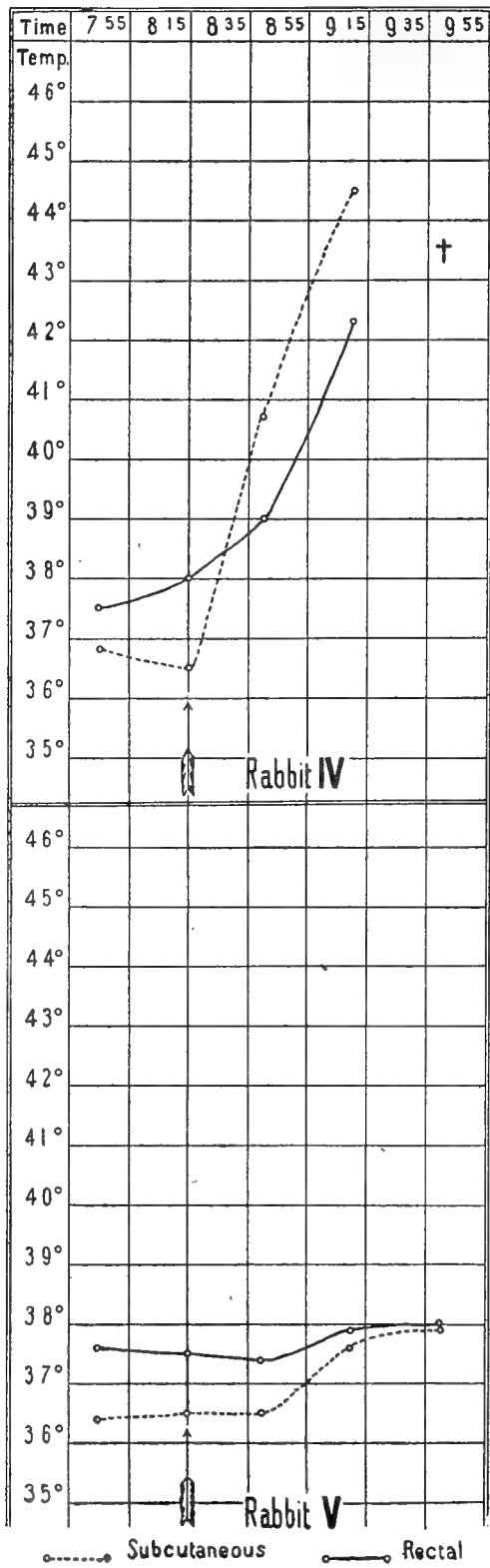


CHART I.



TABLE III.—*Temperature, subcutaneous and rectal of dogs in sun and shade.*

Date.	Remarks.	Time.	Temperature.		Black-bulb thermometer.
			Rectal.	Subcutaneous.	
			°C.	°C.	
1910.		9.00 a. m.	36.9	-----	52°.1 at 11 a. m.
Oct. 5	Brown dog, tracheotomized Oct. 4, 1910. In animal house. Exposed to sun 9.20 a. m.	9.30 a. m.	37.8	-----	
		9.40 a. m.	39.2	-----	
		9.50 a. m.	40.1	-----	
		9.55 a. m.	40.9	44.2	
		10.00 a. m.	41.0	-----	
		10.05 a. m.	42.0	45.5	
	Falls down in lethal condition, taken into room, died 10.40 a. m. (Rectal temperature 41°.)				
Oct. 19	Black dog, tracheotomized Oct. 17, 1910. In animal house. Exposed to sun 9.25 a. m.	9.00 a. m.	38.3	38.0	49° at 11 a. m.
		9.55 a. m.	40.7	42.9	
		10.10 a. m.	41.7	42.9	
	Falls down at 10.10 a. m.; taken into room until 10.30 a. m.; exposed to sun again. Taken into room at 11.15 a. m.; recovers.	11.00 a. m.	41.9	42.5	
		11.15 a. m.	42.8	37.9	
		12.30 p. m.	38.0	37.5	
Oct. 21	Same dog from Oct. 18, 1910. In animal house. Exposed to sun 8.45 a. m.	8.30 a. m.	38.0	37.0	45°.6 at 11 a. m.
		9.15 a. m.	40.0	41.0	
		9.50 a. m.	44.2	44.5	
				died.	

Tracheotomized rabbits, while inside of a room, act normally, but if they are exposed to the sun they die, the body temperature rising more rapidly than with normal rabbits.

The post-mortem findings in the dogs and rabbits which died were: Hyperæmia and a certain number of small hæmorrhages in the subcutaneous tissues, hyperæmia of all internal organs, especially of the brain and the meninges. Several punctiform and linear hæmorrhages could be seen on the surface of the brain, as well as on the dura mater.

I have attempted roughly to estimate from the loss in weight the relative quantities of water evaporated by rabbits in the sun and in the shade. I collected the fæces, urine, and saliva excreted and deducted this amount from the loss in weight of the animal. Of course, the figures obtained in this way are not exact, the carbon dioxide excretion not being taken into consideration, but a comparison between two animals otherwise under the same conditions gives an approximate idea of the loss of water. The calculations are given in Table IV.

TABLE IV.—Loss of weight of rabbits in sun and shade.

Time.	Total number of hours.	In sun.					In shade.				
		Weight.			Urine and faeces collected.	Reduced loss of weight.	Weight.			Urine and faeces collected.	Reduced loss of weight.
		At start.	At end.	Loss.			At start.	At end.	Loss.		
8 to 9.50 a. m.---	h. m. 1 50	Gms. 1,640	Gms. 1,580	Gms. 60	Gms. 18	Gms. 42	Gms. 1,943	Gms. 1,936	Gms. 7	Gms. -----	Gms. 7
2 to 4 p. m. -----	2 0	1,795	1,744	51	10	41	2,148	2,137	11	-----	11
9.30 to 11.45 a.m.	2 15	2,182	2,032	150	35	115	1,730	1,725	5	-----	5

*Reduced per hour and kilo body weight.*

Loss in sun.	Simultaneous loss in shade.
Grams.	Grams.
14	2
12	3
23	2

Cats behave more or less as do dogs or rabbits. Their body temperature rises, and if they are exposed to the tropical sun long enough, they will die.

EXPERIMENTS ON MONKEYS.

Experiments on monkeys promised the best result because these animals are at home in the Tropics. Monkeys, like rabbits and dogs, have no sweat glands, and their physical heat regulation is confined to the reduction brought about by water evaporated from the lungs and mouth by increased respiration. However, this capability to evaporate water is very limited. In my experiments the monkeys were fastened in sunny places in the garden, or on the roof to a small stick by means of a chain around their bodies. The body temperature of the animals exposed to the sun rose within one hour from 38°.5 or 39° to 42° or more. The subcutaneous temperature at the same time reached values of 45° and even 46°. Within seventy to eighty minutes the monkeys died, even if they were exposed to the sun in the early forenoon, between 9 and 10, in December and January. These months are among the coolest in Manila. Even an open umbrella gives sufficient shade to protect the animals from the injurious effects of the sun. I have especially studied the changes of the subcutaneous and rectal temperatures in monkeys and the relation between these two values deserves attention. The subcutaneous temperature in a normal monkey inside the house and for the greater part in the shade is somewhat below the rectal. As soon as the animals are placed in the sun, the subcutaneous temperature rises above the rectal, and, until the end of the experiment, exceeds the latter. The interior of the body is warmest in normal animals and becomes

cooler toward the periphery. In the sun, on the contrary, the body is hottest on the outside and cooler toward the inside, the latter now receiving heat from the periphery. As a result of this condition the temperature measured *in ano* in a normal animal is very nearly the same as that of the blood and surrounding tissues, but in monkeys exposed to the sun, it will lie, in all probability, below that point. The parts of the body nearest the periphery will show a temperature almost the same as the subcutaneous, the more central portions a temperature between the rectal and subcutaneous. Experiments may be mentioned in this connection in which two monkeys were exposed to the sun, the one with its normal coat of hair, the other, shaved all over. The temperature of the shaved animal rose much more rapidly than that of the other. On the other hand, in the shade or inside a house, the shaved animal has a slightly lower body, and a decidedly lower subcutaneous temperature. The explanation is clear when we consider the fact that the coat of hair protects both against loss of heat by conduction and an increase from radiation.

The following characteristic examples of protocols illustrate these points and they are even more plainly brought out by the temperature charts.

TABLE V.—*Experiments with normal and shaved monkeys.*

Date.	Remarks.	Time.	Temperature of—								Black-bulb thermometer.
			Monkey II exposed to sun.		Monkey X in shade of umbrella.		Monkey XI in normal hair coat exposed to sun.		Monkey XII, shaved, exposed to sun.		
			Sub-cutaneous	Rectal.	Sub-cutaneous	Rectal.	Sub-cutaneous	Rectal.	Sub-cutaneous	Rectal.	
1910. Nov. 16	In animal house. Exposed to sun 9 a.m.	8.50 a.m.	38.1	38.0	—	—	—	—	—	—	52°
9.15 a.m.		39.8	42.0	—	—	—	—	—	—		
9.30 a.m.		41.0	44.0	—	—	—	—	—	—		
9.45 a.m.		42.0	44.0	—	—	—	—	—	—		
10.00 a.m.		43.9	44.8	—	—	—	—	—	—		
10.08 a.m.		43.9	—	—	—	—	—	—	—		
Slight cramps, forced and slow respiration, saliva dropping, 10.10 a. m. died.											
1911. Jan. 18	In animal house. Exposed to sun 2.25 p.m.-----	2.05 p.m.	-----	-----	37.5	38.5	38.1	38.4	36.6	37.9	-----
2.35 p.m.		-----	-----	39.2	39.4	40.4	39.9	40.9	-----	-----	
2.40 p.m.		-----	-----	-----	-----	-----	-----	-----	40.6	-----	
2.55 p.m.		-----	-----	-----	-----	-----	-----	44.6	43.8	-----	
2.60 p.m.		-----	-----	-----	-----	43.2	41.4	44.8	44.0	-----	
3.05 p.m.		-----	-----	39.6	39.8	-----	-----	45.5	44.4	-----	
3.10 p.m.		-----	-----	-----	-----	43.8	41.4	-----	Died.	-----	
3.20 p.m.		-----	-----	-----	-----	-----	41.6	-----	-----	-----	
3.35 p.m.		-----	-----	40.3	-----	44.4	-----	-----	-----	-----	
3.45 p.m.		-----	-----	-----	-----	-----	42.3	-----	-----	-----	
3.50 p.m.		-----	-----	40.2	40.5	-----	-----	-----	-----	-----	
4.00 p.m.		-----	-----	-----	-----	44.5	43.4	-----	-----	-----	
4.15 p.m.	-----	-----	40.0	40.1	45.4	{ 44.1 died. }	-----	-----	-----		

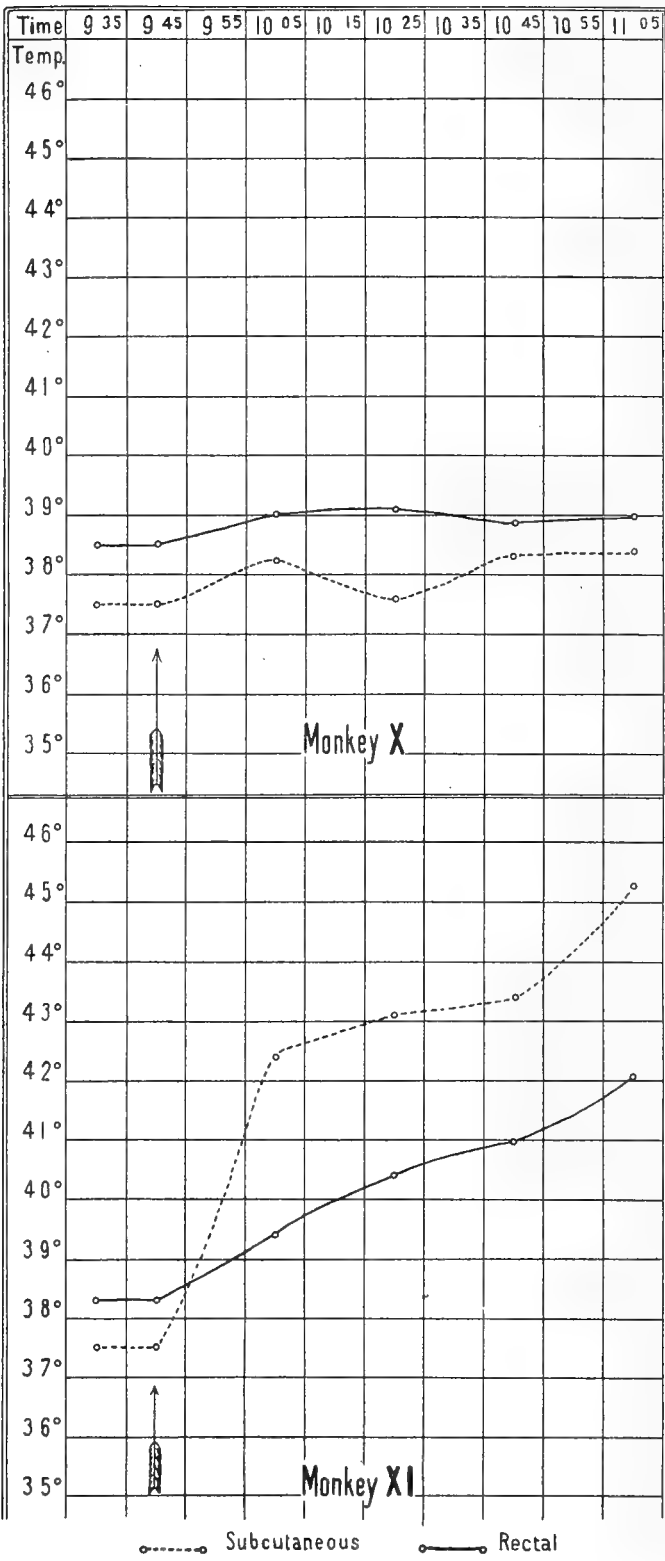


CHART II.

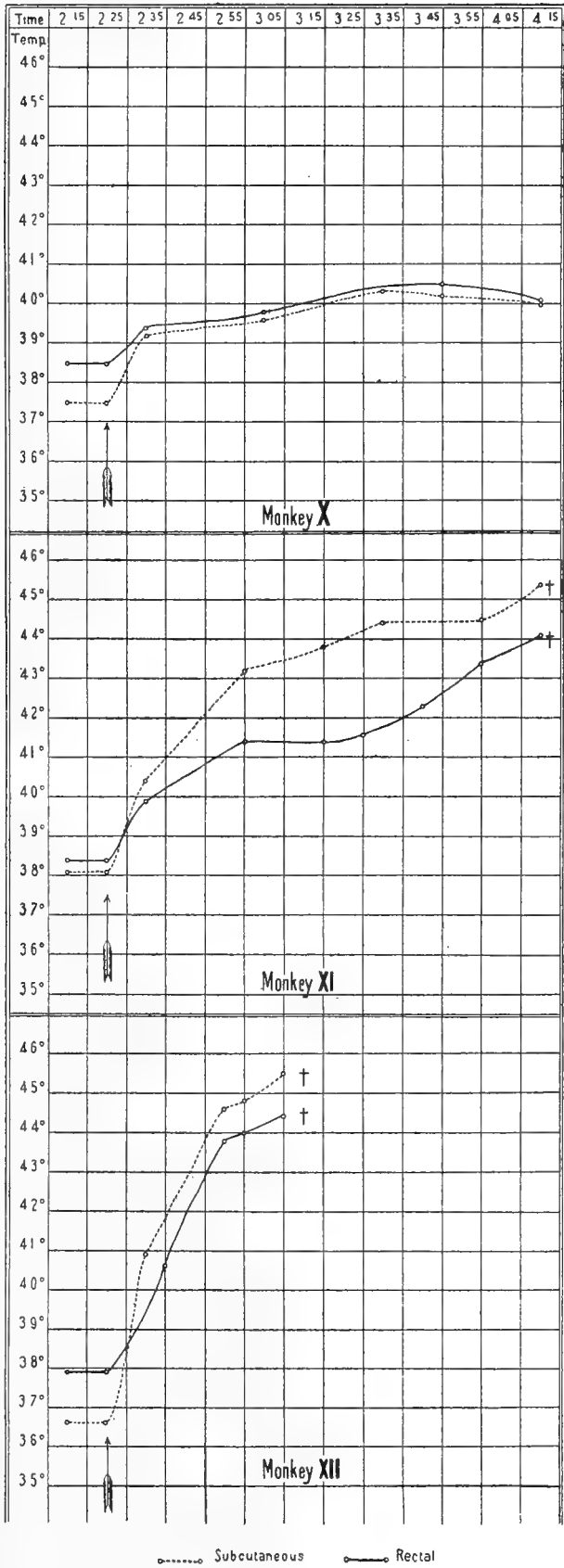


CHART III.

The following experiments were arranged in order to show beyond doubt that hyperthermia alone must be regarded as the true cause of the death and of the injurious effects brought about by the radiation of the sun.

Monkeys were exposed to the sun, while at the same time a strong current of air from an electric fan was blown over their bodies. Under these conditions the temperature did not rise in the same degree as in a control animal exposed at the same time, but outside the influence of the fan. Monkeys in the sun but exposed to the wind behaved more or less as did the animals under an umbrella or in the shade, no injurious effects from the sun's rays being noticed, because the motion of the air increased the loss of heat. When placed under the fan, the animals lost the excessive heat which reached them by radiation from the sun. The rays, including the ultra-violet, were nevertheless present and were absorbed by the body in the same manner and degree as by that of the control monkey. Table VI and Chart IV make the above experiments clear.

TABLE VI.—*Monkeys in the sun, with and without a blast of air from a fan.*

Date.	Remarks.	Time.	Temperature of—									
			Monkey X in sun and wind.		Monkey XIII in sun and wind.		Monkey XIII in sun alone.		Monkey XIV in sun and wind.		Monkey XIV in sun alone.	
			Sub- cuta- neous	Rec- tal.	Sub- cuta- neous	Rec- tal.	Sub- cuta- neous	Rec- tal.	Sub- cuta- neous	Rec- tal.	Sub- cuta- neous	Rec- tal.
1911.		a. m.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
Jan. 24	In animal house.....	9.50	-----	-----	37.9	38.6	-----	-----	-----	-----	38.7	38.9
	Exposed to sun 10 a. m. ....	10.15	-----	-----	37.5	39.4	-----	-----	-----	-----	41.5	40.3
	Interrupted .....	10.30	-----	-----	-----	39.3	-----	-----	-----	-----	-----	40.9
Jan. 26	In animal house.....	8.30	-----	-----	-----	39.5	-----	-----	-----	-----	-----	38.5
		8.45	-----	-----	38.6	-----	-----	-----	-----	-----	37.3	-----
	Exposed to sun 9 a. m. ....	9.15	-----	-----	39.3	39.8	-----	-----	-----	-----	40.6	39.7
		9.30	-----	-----	38.6	40.0	-----	-----	-----	-----	41.1	41.0
		9.45	-----	-----	39.2	40.3	-----	-----	-----	-----	42.2	41.8
		10.00	-----	-----	38.7	40.2	-----	-----	-----	-----	-----	42.5
	Interrupted .....	10.10	-----	-----	-----	40.1	-----	-----	-----	-----	43.5	42.7
	In animal house.....	10.30	} 36.8	38.2	-----	-----	38.1	39.0	38.5	39.4	-----	-----
		10.45										
	Exposed to sun 10.50 a. m. ....	11.10	-----	39.3	-----	-----	-----	40.3	-----	39.8	-----	-----
		11.20	37.2	-----	-----	-----	42.7	-----	39.1	-----	-----	-----
		11.30	-----	39.6	-----	-----	-----	42.4	-----	40.1	-----	-----
		11.40	39.5	-----	-----	-----	44.8	-----	40.8	-----	-----	-----
		11.50	-----	40.5	-----	-----	46.3	{ 44.8 { died.	-----	40.4	-----	-----
	p. m.	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		1.00	-----	*39.8	-----	-----	-----	-----	-----	*40.6	-----	-----

\* Left in sun under fan.

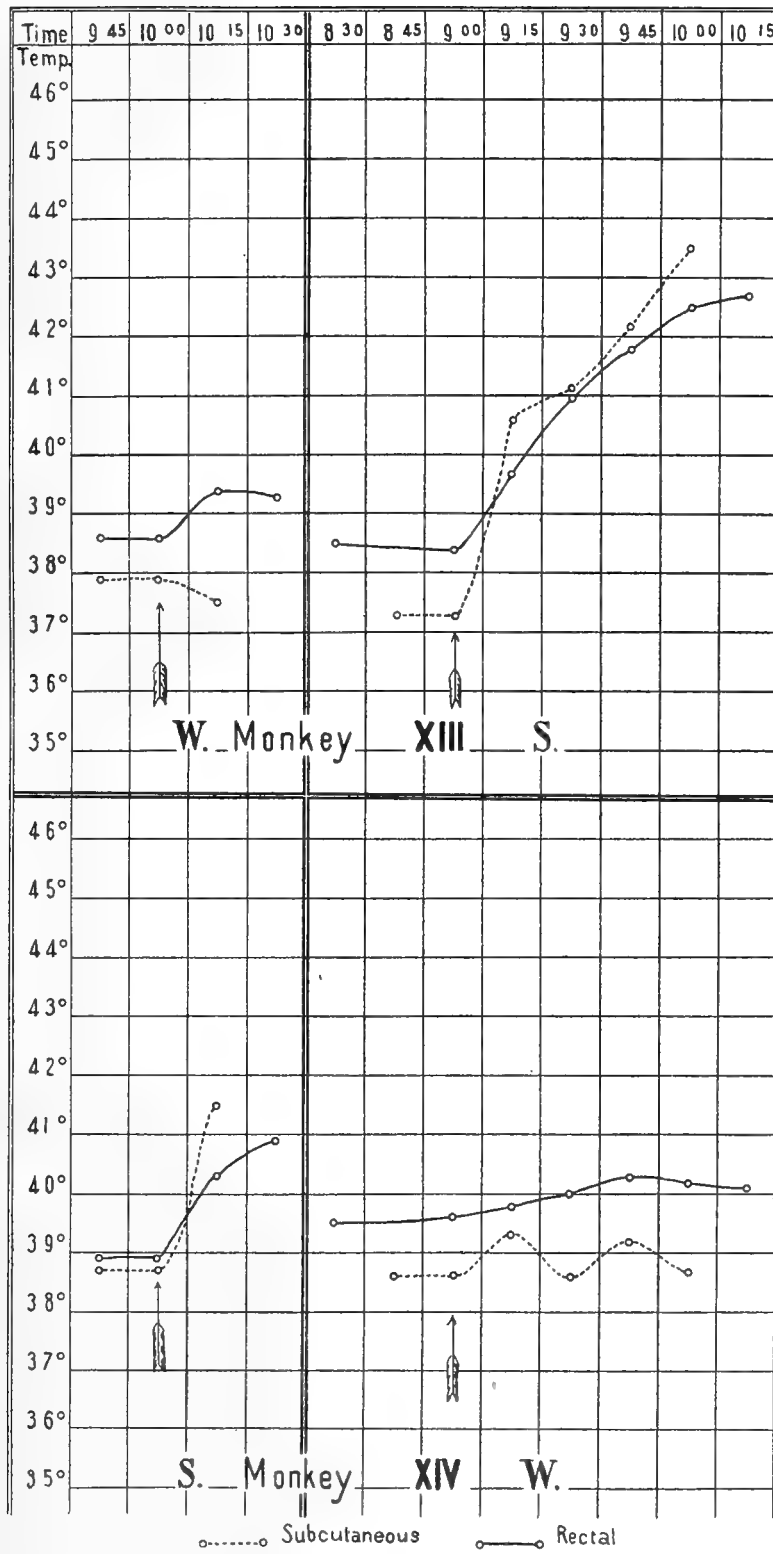


CHART IV.

I have exposed the heads only of monkeys, by placing their bodies in a large wooden box 33 by 33 by 50 centimeters, the top of the box being fitted closely around the neck of the animal. Several holes were made in its walls to allow a free circulation of air, and, finally, the first box was placed inside a second, larger one, 50 by 50 by 48 centimeters. In this way the body was in the shade and well protected against the rays of the sun, while the head was unprotected. Monkeys have been exposed in this way for several days, from morning to afternoon, without any effect. One monkey, number 6, was insulated in this way for a total of fifty-four hours in twelve days, and the animal is still well and healthy. Temperatures up to  $47^{\circ}$  were measured in the hair of the head during several exposures, but the rectal and subcutaneous temperatures of the animal never went above the normal.

P. Schmidt<sup>19</sup> assumes that the heat rays from the sun, although partly absorbed by the skin and bone of the skull, at least in part penetrate the brain, and the latter organ, being very sensitive to an increase of heat, will not withstand the effects of the rays.

In my experiments with the monkeys in the box the heat rays could penetrate freely to the brain. The fact that the radiation reaches the skull appears to have no effect, if the body temperature does not rise at the same time.

Deleterious effects are only observed when the body temperature rises to febrile heights, but if this rise is prevented by a strong current of air or by protecting the greater part of the body against the heat rays, the animal will not suffer from radiation from the sun.

Post-mortem findings on monkeys dying after exposure to the sun, give the following characteristics:

Hyperæmia of the subcutaneous vessels and of all internal organs. In two monkeys small hæmorrhages in the subcutaneous tissues and in some of the muscles are observed. I can not exclude injury from the chains with which the animals were fastened as a cause of the latter condition. The alterations in heart and brain are of greater interest: All monkeys<sup>20</sup> which die after exposure to the sun show extensive hæmorrhages in the muscular wall of the left ventricle. These hæmorrhages are situated beneath the endocardium and for the greater part near the auriculo-ventricular border, sometimes they are also in the papillary muscles. Their extent and number varies somewhat, the smallest are rectangular, 3 by 2 millimeters. Considering the size of a small monkey's heart, these are quite severe alterations. The vessels of the dura mater are far more distended than with normal monkeys, and at several places small hæmorrhages are found. The arachnoidea is slightly raised by an exudate lying

<sup>19</sup> *Loc. cit.*

<sup>20</sup> This protocol is based on seven animals.



between it and the brain. The blood vessels of the brain are very hyperæmic; fresh, small hæmorrhages are found in several places on the basal side of the frontal lobe.

There can be no doubt but that the changes in the brain and the lesions of the heart described above were fresh and characteristic of the effects of the sun. (See Plates I and II.)

The following seems to me to be the most probable interpretation of our observations on monkeys, dogs, rabbits, and cats. The heat radiated from the sun warms the body tissues more rapidly than can be compensated for by the regulatory organism of the body. The tissues and the blood increase in temperature to a point higher than is compatible with life. Apparently the organs most susceptible to this increased heat effect are the brain and heart. It is undecided whether the lesions in the brain or heart are the most essential in causing death.

The most important fact shown by these experiments is that the outer parts of the body are heated by the sun to a greater extent than the interior. Therefore, I next endeavored to ascertain the effect of the rays of the tropical sun upon the temperatures of the skin of man.

I have not found any account of experimental work done in this line. Däubler<sup>21</sup> discusses the skin temperature and shows the necessity of investigations in the Tropics. The only fact which need be mentioned here is a statement by Schilling. This investigator placed a thermometer between the teeth and cheek in the mouth of a man. In the room, the thermometer showed 36°.6. The man exposed his face to the sun when the sunshine thermometer registered 55°, the thermometer in his mouth rose to 37°.05.

#### THE TECHNIQUE OF THE EXPERIMENTS.

Mercury thermometers, even if especially constructed for taking the skin temperature, are not suitable for this work because it is impossible to protect such instruments against the radiation of the sun. The only method suited to taking exact measurement of skin temperatures is thermoelectric, as it has been applied by Kunkel<sup>22</sup> and Rubner, Kisskalt,<sup>23</sup> Reichenbach, and Heymann<sup>24</sup> in the study of the normal skin temperature in men. The greatest difficulty to be overcome in the construction of such an apparatus for our studies was to keep the secondary place of junction of two metals at a constant temperature, even in the sun, and to avoid disturbing currents produced by changes in temperature of any junction between two different metals in any part of the circuit outside the thermocouple proper used for the measurements.

<sup>21</sup> Die Grundzüge der Tropenhygiene, Berlin, 1900.

<sup>22</sup> *Ztschr. f. Biol.* (1889), 25, 55-91.

<sup>23</sup> *Arch. f. Hyg.* (1909), 70, 17-39.

<sup>24</sup> *Ztschr. f. Hyg. u. Infektionskrankh.* (1907), 57, 1-22.

This danger is avoided by introducing two thermocouples in opposite directions in such places, the one neutralizing the other. If care is now taken to keep two such junctions ( $x$  and  $y$ ) at equal temperatures, absolute changes in temperature will not produce current from such junctions. This is shown by the following figures, in which Scheme I shows the usual arrangement and Scheme II that employed by me.

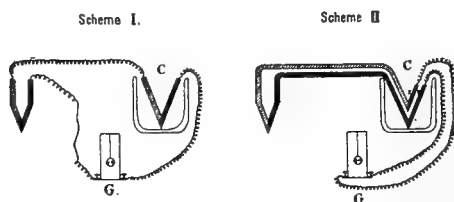


FIG. 1.

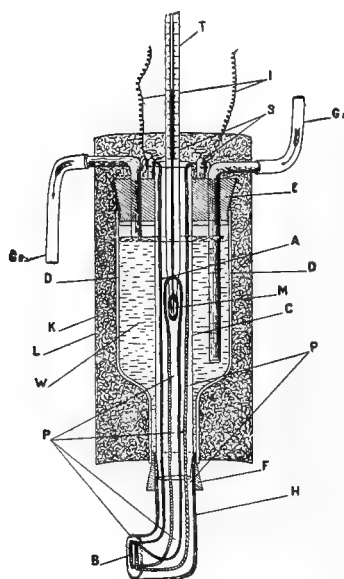


FIG. 2.

According to this principle I have constructed an apparatus suitable for taking skin temperatures, and also others for taking temperatures inside of clothing or under the skin or even in the rectum of a monkey. Figure 2 is a diagram of the thermocouple used.

Constantan in the form of wire (black in the figure) and iron wire (dotted in the figure) each of 1 millimeter diameter were soldered together. The junction at A was kept at a constant temperature which could be read to  $0^{\circ}.1$  by means of a sensitive normal thermometer T, the mercury bulb of which M was at the same point as A. Both wires were hammered to a fine leaf of about 0.1 millimeter thickness at the "thermometric" junction B and soldered together so that two fine plates resulted, which were carefully cleaned from all superfluous solder by sandpaper. These were placed exactly in the same level. This system of wires, surrounded by silk and insulation tape, was inclosed in its upper two-thirds in a glass tube C fitted in its lower one-third into a wooden box H of the shape of a tobacco pipe. The lower part of the glass tube and the wooden box were filled in with melted paraffine P. The lower end of the paraffine was formed into a block, the leaf-like junction B being carefully cleaned from all paraffine, so that there was left only a minute space between B and the paraffine block P. The glass tube C was now inserted into another, larger tube D by means of two rubber stoppers, E and F, E having three holes, one for D and the other two for two glass tubes  $G_1$  and  $G_2$ , which served to circulate water. The iron wires coming from A were fixed in two pole screws S on the upper end of the glass tube C. The wires, I, led to the galvanometer. Finally, D was covered with a layer of felt and cotton K and inclosed in a cylinder of white carton paper L.

Water entering at  $G_1$  and leaving at  $G_2$  kept the temperature of the secondary couple A constant even in the hottest sun.  $G_1$  was connected by a rubber tube about 3 to 4 meters in length with a tank containing 50 liters of water. The copper wires, I, with a strong coat of yellow silk insulation were coiled in the usual manner. The measurements were taken on a flat roof, while the galvanometer, connected by means of a copper key, and the wires, I, were inside the room, protected from the sun. The apparatus was freely movable and served the purpose well. I will not designate the form as ideal, but it must be remembered that it was entirely built in Manila.

The galvanometer was of the d'Arsonval principle, formerly used at the Weather Bureau and kindly loaned to me by the Rev. José Algué, S. J.

Series of test experiments were made when the apparatus was complete. B was immersed in oil baths of different temperatures in one series, in another it was inclosed in a tube fitted with a thermometer and immersed in water, the temperature of which was varied. In a third series the temperature of A was changed and that of B kept constant. Of course, all the wire connections, the galvanometer, the scale, and the position of the telescope were kept unchanged. One division of my tangential scale was equal to  $0^{\circ}.19$  of the thermometer, and half of this interval could be read exactly and quarter intervals approximated. Readings were therefore correct to  $0^{\circ}.1$ . The deflection of the galvanometer was directly proportional to the change in temperature if the temperature limits were not greater than  $8^{\circ}$  or  $9^{\circ}$ , equal to about 40 parts on my scale.

The second type of apparatus is shown in figure 3. One constantan wire and one iron wire were soldered together. The place A was to be kept at constant temperature, and B to serve as the thermometric junction. Here the wires were hammered to fine leaf and soldered together in the form of a very flat V. They were insulated by tape and covered with a layer of silk and oilcloth. A was fixed on the mercury bulb M of a thermometer T and inclosed in a tin cylinder C so that the wires did not touch the tin box C. Two copper wires I led from the iron to the galvanometer, the places of junction between iron and copper being kept at the same temperature. The tin box C was placed in a Dewar vacuum-jacketed vessel of about 300 cubic centimeters capacity, which was filled with oil O. The Dewar vessel, resting on a piece of bamboo E, was placed in a large glass jar F which was filled with carbon K. The Dewar vessel was closed by a cork stopper G, having holes for the thermometer and the four wires. The carbon was covered by a cylindric cardboard H, which latter was covered with cotton. The two wires of constantan and iron in this drawing are shown shorter than in the apparatus, the place B was freely movable and 1 meter distant from the jar F which was kept under a large wooden box. The temperature of A was constant for one hour or more at  $0.01$ . Test experiments were performed for each apparatus at varying intervals by placing B in oil baths of different temperatures. One division of my galvanometer scale corresponded to  $0^{\circ}.423$  on the thermometer in the apparatus I used most, so that the sensitiveness of this thermocouple was less than one-half of that used for measuring the skin temperatures. Thus, larger temperature variations, accurate to  $0^{\circ}.2$ , could be recorded with this second type of apparatus.

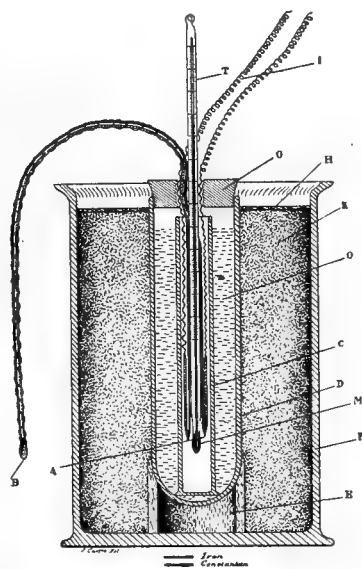


FIG. 3.

A few words are necessary concerning the technique of taking the skin temperature. Two persons must coöperate in making the measurements, one reading the galvanometer, the other handling the thermometric apparatus. The latter work was performed by a clever native

of long training, who was also able to read the galvanometer. However, I generally preferred to do this more responsible part of the work myself.

After adjusting the apparatus, taking the zero point of the galvanometer and being sure that the place of junction was being kept for at least five minutes within  $0^{\circ}.1$ , the thermometric junction was warmed in the palm of the hand and then placed on the different parts of the skin, which were to be measured. The metal leaf must just slightly touch the skin, and must be kept at one place until the galvanometer just reaches its maximum deviation; with my apparatus twenty seconds was almost more than sufficient for this purpose. Especially in experiments conducted in the sun, the place to be measured must not be touched too long, because the thermometer itself casts some shade. According to Kunkel's suggestion I have measured falling as well as rising temperatures, but I observed no difference between them.

It is more tedious to take the temperature in the hair or under clothes. Here a thermocouple of the second type must be left for three or four minutes until the maximum of deflection is reached. Care must be taken to have the metal well covered by hair in taking the temperature of the air in the hair.

The skin temperatures at different parts of the body, especially that of the head and arms, were first measured on a number of people, both white and brown, inside of a room and also in a shady place outdoors. The values obtained vary within the extreme limits of  $31^{\circ}$  to  $34^{\circ}$ , the greater part of the skin showing temperatures between  $32^{\circ}.5$  and  $33^{\circ}.5$ . The values given by Kunkel for a room temperature of  $20^{\circ}$  are nearly  $1^{\circ}$  higher on an average than those of Rubner for temperatures of  $25^{\circ}.6$  and  $26^{\circ}.5$ , and then my figures are for room temperatures of  $26^{\circ}$  to  $30^{\circ}$ . My figures agree very well, on an average, with those of Reichenbach and Heymann. Different places on the skin do not have exactly the same temperature; that over thicker muscular parts or over abundant fat being always higher, often as much as  $1^{\circ}$ , than that found in places where the bones lie closely under the skin. This is very pronounced over the malar bones, and on the hand. The highest temperatures generally occur on the forehead and neck; the palm of the hand is always warmer than the back, and similar variations occur in other parts of the body. Care should be taken always to measure the temperature on a dry skin; wet skin gives different values. Table VII shows normal values for the skin temperatures as obtained from a number of experiments on different people. The values given by Rubner and Kunkel are placed beside them for comparison.

TABLE VII.—Skin temperature.

Subject.	Place.	Palm of hand.	Back of hand.	Finger.	Finger nail.	Fore-arm out-side.	Fore-arm in-side.	Cheek over malar bone.	Tip of nose.	Fore-head.	Lobe of ear.	Chest.
C	In room 29° 5	33.4	32.6	33.0	32.3	33.3	33.3	33.3	33.1	32.8	32.3	33.8
A	In room 29° 2	33.3	32.9	33.1	31.7	33.0	32.7	33.2	32.9			
T	In room 29° 0	33.3	32.6	32.5	32.1	32.9	32.7	33.5	33.3	33.9	31.7	33.7
S	In shade outside 28°		30.7			32.8		32.8		33.4		
A	In room 26°	33.2	32.8	32.6	31.1	32.8	32.6	33.0	31.7	33.6	30.3	33.2
T	In shade outside 25°		{ 31.0— 31.4 }			31.8	31.4	31.2		32.4		
F	In room 30° 1					32.8	32.4	33.2	33.4	33.9		
C	In shade outside 27°		32.1			32.5		31.9		33.6		
Mc	In room 26°	32.8	32.6	32.5	30.5	32.4	33.2	32.2	33.3	33.8	30.3	33.5
Mo	In room 26°	32.4	32.2	31.6	30.9	33.0	33.0	32.4	33.6	33.9	30.7	33.3
Kunkel	Room temperature, 20°	{ 34.4— 34.8 }	{ 32.5— 33.2 }			33.7		34.1		{ 34.1— 34.4 }	23.8	34.4
Reichenbach and Heymann	One subject, room temperature 34°		33.6	34.1				35.8	35.0	34.6		
	Two subjects, room temperature 29°		{ 33.2— 33.8 }	32.3				34.0	33.3	33.5		
	Three subjects, room temperature 26° 6		{ 33.7— 34.1 }	33.7				34.1	33.6	35.0		

TABLE VII.—*Skin temperature*—Continued.

RUBNER.

Room temperature-----	25°.6.		26°.5.	
Individual -----	N.	R.	Rbch.	R.
Angle of nose -----	31.0	31.3	33.1	32.7
Eyelid-----	32.0	33.1	33.8	33.6
Hand-----	31.0	32.0	33.1	32.3
Skin-----	33.0	33.0	-----	-----

I proceeded in different ways in order to study the influence of the radiation of the sun on the skin temperature. I placed a man in a sunny place in such a way that half of his face and body were exposed to the sun rays, the other side being in the shade, and the temperatures of corresponding places of both sides of the body were taken. Another arrangement was the following: The skin temperatures of several places on the skin were taken in the shade, the spot where the highest temperature of a certain region was found was marked by a very fine mark and the subject then placed in the sun, in some experiments sitting, in some lying on a cot. The temperature of the same marked places was again determined at different intervals of time after exposure. In several sets of observations I have studied a Filipino and a white man side by side.

The results of the insolation experiments are as follows: The naked human skin if exposed to the rays of the sun is warmed very quickly to about 36°. If one side is kept in the shade, the other exposed, the difference in temperature on the two sides may amount to 3°. (See Table VIII.) Above 36°, in a maximum 37°, the temperature of the skin no longer increases; on the contrary, if the exposure is continued, the temperature falls. This fall is more or less coincident with the outbreak of sweat, and the greater the secretion of sweat, the greater the fall in the temperature of the skin. The fall in skin temperature is more decided if the sweat secretion is increased by performing muscular work in the hot sun. (See Table VIII.)

TABLE VIII.—Characteristic records of experiments testing human skin temperature radiated by the sun. Figures, except pyrhelimeter readings, in degrees centigrade.

[Fr. Filipino, upper half without clothes ten minutes in sun. Sunny side, 35°.8 to 36°.3; shaded side, 32°.1 to 32°.4.]

JANUARY 4, 1911.

(Pyrhelimeter reading 9.20 a. m., 680; 9.40 a. m., 720.)

T. American, brown hair.	Side measured.	Arm.	Cheek.	Forehead.	Chest. <sup>a</sup>
Air temperature in shade 24°.2	-----	31.4 to 31.8	31.0 to 31.2	31.0 to 32.4	32.9
Air temperature in shade 24°.7. One side of face 10 to 15 minutes in sun, other side in shade, corresponding points.	Sunny side	35.8	35.2	-----	41.8
	Shady side	31.5 to 31.9	31.3 to 31.9	31.7 to 31.9	-----

<sup>a</sup> Between shirt and undershirt. Air in hair after exposure 46°.0.

JANUARY 6, 1911.

Ma. Filipino.	Face.	Forehead.	Palm of hand.	Back of hand.	Chest.
Muscular work in sun, severely perspiring -----	32.4 to 32.9	33.5 to 33.7	33.3 to 33.9	32.8 to 33.1	33.9 to 34.5

JANUARY 3, 1911.

(Pyrhelimeter reading 10 a. m., 845; 10.30 a. m., 865.)

Ma. Filipino.	Face.	Forehead.	Arm.	Tip of nose.	In hair.	Chest.
Air temperature in shade 28°.9-----	31.5 to 31.9	32.5	32.1 to 32.5	31.7	-----	32.5
After 30 minutes in sun -----	35.4	34.9	36.9	34.1	44.0	39.8

JANUARY 10, 1911.

(Pyrhelimeter reading 9.30 a. m., 845; 9.40 a. m., 850.)

Individual.	Condition.	Arm.	Hand.	Forehead.	Cheek.	In hair.	Axilla. <sup>a</sup>
S. American, fair hair.	In shade 28° -----	32.8	<sup>b</sup> 30.7	33.4	32.8	35.2	-----
	After 15 minutes in sun, sweat in fine droplets.	35.6	35.6	34.8	34.0	44.1	37.6
F. Filipino, brown skin, black hair.	After 15 minutes in sun, same day, directly after S.	33.4 to 34.8	34.6 to 34.8	34.3	33.9	46.7	-----

<sup>a</sup> Between shirt and undershirt.

<sup>b</sup> Has wet hands.

TABLE VIII.—Characteristic records of experiments, etc.—Continued.

JANUARY 9, 1911.

(Pyrheliometer reading 9.35 a. m., 840; 9.45 a. m., 855.)

The same marked points were measured.

Individual.	Condition.	Face.	Fore head.	Arm.	Hand.	Neck (back)	In hair.	Axilla.
Gz. Spanish mestizo, white skin, hair dark brown.	In shade 10.30 a. m. Air temperature 27°.	32.4	33.4	33.0	32.8	33.0	32.1	-----
	11.15 a. m. after 25 to 30 minutes in sun (slightly sweating).	36.5	36.3	37.1	36.5	35.0	46.8	-----
	11.30 a. m. after muscular work in sun, freely sweating.	33.0	32.4	33.2	33.0	34.0	-----	-----
Cs. Filipino, dark brown skin, black hair.	10.30 a. m. as above -----	32.6	33.8	32.8	31.6	33.2	37.4	36.3
	11.15 a. m. as above -----	36.3	36.1	36.3	35.5	34.6	46.8	38.7
	11.30 a. m. as above -----	32.6	33.6	33.4	31.8	32.8	-----	-----

° Not directly in sun.

JANUARY 17, 1911.

(Pyrheliometer reading 9.40 a. m., 750.)

Individual, the same, lying on field bed.	Condition.	Arm.	Hand.	Fore-head.	Face.		Neck.	In hair.	Axilla.
					Cheek.	On malar.			
Gz. Spanish mestizo, white skin, hair dark brown.	9.50 a. m. in shade air temperature 27 to 27° 5.	32.5	32.7	33.3	33.1	32.7	33.7	27.8	36.3
	10.05 a. m. 10 minutes in sun.	36.2	35.8	36.2	35.2	34.8	35.4	-----	37.4
	10.25 a. m. 30 minutes in sun.	35.0	35.0	35.4	35.6	35.4	35.0	41.2	38.2
	10.55 a. m. 1 hour in sun.	34.6	34.6	35.4	35.2	35.0	35.0	47.9	39.7
Cs. Filipino, dark brown skin, black hair.	9.50 a. m. as above -----	32.3	32.5	33.5	32.9	31.9	33.3	28.2	-----
	10.05 a. m. as above -----	36.2	34.2	35.6	34.1	34.4	34.8	-----	-----
	10.25 a. m. as above -----	35.0	34.2	34.8	34.4	34.2	34.4	44.2	-----
	10.55 a. m. as above -----	34.8	34.2	34.8	34.8	34.6	34.4	50.1	-----



TABLE VIII.—Characteristic records of experiments, etc.—Continued.

JANUARY 28, 1911.

Individual.	Time.	Arm.	Cheek.	Fore-head.	Neck.	In hair.
B. American, brown hair	9.45 a. m. in shade	32.5	33.3	33.9	34.1	33.1
	9.50 a. m. exposed to sun					
	9.55 a. m. exposed to sun	34.7	35.9	35.5	36.8	
	10 a. m. exposed to sun	35.5	36.6	36.4	37.0	39.1
	10.10 a. m. exposed to sun	35.7	37.4	35.9	36.8	38.9
	10.20 a. m. exposed to sun	36.9	36.3	35.6	36.5	
Or. Filipino, dense black hair.	9.45 a. m. in shade	33.4	34.0	34.4	34.2	32.7
	9.50 a. m. exposed to sun					
	10 a. m. exposed to sun	37.2	36.6	35.9	35.7	43.4
	10.10 a. m. exposed to sun	37.2	36.4	35.9	35.7	44.0
	10.20 a. m. exposed to sun	36.1	35.4	35.2	35.4	

The figures given for pyrheliometer values are the number of milliamperes necessary to produce the current which warms one German silver leaf to the same temperature as the other exposed to the sun. They do not give absolute figures (see discussion, p. 119), but they indicate thus far the relative value of the radiation of the sun on the different days. Only clear days were chosen for experiments, and but slight differences in the radiated heat of the sun were found.

The temperature in the hair of an uncovered head increases to much higher values than those of the skin, and here no fall is observed. The color of the hair, as well as its thickness, is of great importance. In the black, dense hair of a native of the Philippines, the temperature may rise to 50°.1 within one hour, and approximately 45° as a rule is obtained within thirty minutes.

Kunkel states that he has never observed skin temperatures above 35°.5. In the tropical sun I have obtained slightly higher values, the highest being 37°.4, but generally 36°.5 was the upper limit.

Table IX shows a comparative study of the behavior of white and brown skin. In the sun, the white skin is always slightly hotter than the brown and with the brown skin the fall in temperature after a certain time of exposure is more pronounced. The heat absorbed by a brown skin is greater than the heat absorbed by a white skin in the same length of time. Therefore, it would seem as if the rise in temperature should take place more quickly in colored than in white skin. This has been experimentally proved to be true with dead skin by P. Schmidt<sup>25</sup> and Eykmann.<sup>26</sup> Yet, just the reverse is true in living men. Brown skin will absorb a greater quantity of rays than white, but being more quickly heated, the point where sweat secretion begins is reached earlier, and as soon as this point is reached the skin is cooled by water evaporation. With the white skin, this process takes place more slowly and it

<sup>25</sup> *Loc. cit.*<sup>26</sup> *Virchows Arch.* (1895), 140, 125-157.

must be for this reason that the brown skin, while absorbing more heat, is found to have lower temperatures than the white skin under similar conditions. The regulatory apparatus of the brown is more sensitive and works more promptly and successfully. This statement deserves attention, because the experiments on dead skin only served to convey a wrong impression of the behavior of colored and white skin when exposed to the sun's rays.

TABLE IX.—*Comparative increase in temperature of white skin and brown skin when exposed to sun, as obtained in the three foregoing experiments.*

Time in minutes.		Temperature of cheek.					
In sun.	In shade.	I.		II.		III.	
		White.	Brown.	White.	Brown.	White.	Brown.
		°C.	°C.	°C.	°C.	°C.	°C.
0	0	32.4	32.6	33.1	32.9	33.3	34.0
10	-----			35.2	34.1	36.6	36.6
20	-----	36.5	36.3	-----	-----	37.4	36.4
30	-----			35.6	34.4	36.3	35.4
40	-----	<sup>a</sup> 33.0	<sup>a</sup> 32.6	-----	-----	-----	-----
50	-----			-----	-----	-----	-----
60	-----			35.2	34.8	-----	-----
		Temperature of forehead.					
0	0	33.4	33.8	33.3	33.5	33.9	34.4
10	-----			36.2	35.6	36.4	35.9
20	-----	36.3	36.1	-----	-----	35.9	35.4
30	-----			35.4	34.8	35.6	35.2
50	-----	<sup>a</sup> 32.4	<sup>a</sup> 33.6	-----	-----	-----	-----
60	-----			35.4	34.8	-----	-----

<sup>a</sup> Muscular work.

It is a matter of general observation that, at a time when the white man is perspiring over his entire body and the sweat is dropping from his face and forehead, the brown man shows only a fine, velvet like layer on his skin. It is not the sweat which *we see*, but that which we do *not see* which exerts the cooling effect; in other words, the water *evaporated*, not the water *secreted* is of value. Sweat which drops is water lost from the body without the corresponding cooling effect. There is economy in sweating, and the most economical way is to secrete no more water than can and will be evaporated. Hypersecretion is useless, and it deprives the body of water. It seems to me that the brown man is superior to the white in this economy of sweating, and we find an expression of that superiority in the lower skin temperature of the brown man in the sun. It is as yet undecided whether the result is due to the color, or if the nervous regulation of the sweat glands, or

even the anatomic build of the latter, is not different in the tropical races from that of white men. Däubler states that the negro has larger and better developed sweat glands than the white man. The fact that Rubner could not find greater water evaporation in negroes than in Europeans at high air temperatures does not contradict my supposition, for, if I am right, the dark skin is superior to the white only in the sun, where radiated heat is absorbed more intensively by the one than the other.

Certain parts of the body, in brown as well as in white men, seem to sweat earlier and more intensively than others. For instance, the forehead always secretes sweat earlier than the arm. As a result, the temperature on the forehead has begun to fall while that of the arms is still rising. In the sun the ultimate temperatures observed on the arm are generally higher than those on the forehead.

The results obtained so far indicate that the temperature of the human skin increases in the sun, but does not reach the normal body temperature. In animals without sweat glands, the skin temperature rises above febrile heights and the tissues lying underneath are heated. On the other hand, penetration of heat through the human skin seems improbable, the effect of the rays absorbed being neutralized by water evaporation on the skin. The more perfect this water evaporation is, the better the normal body temperature may be maintained. The behavior of normal dogs as compared with those which have undergone tracheotomy shows this fact plainly. Monkeys exposed to the sun in Manila die in little over one hour because of their limited capacity to evaporate water, while man, with his well-developed sweat glands resists the same climatic conditions for a much longer period without detriment.

My experiments demonstrate the enormous physiologic and hygienic importance of ample water evaporation in the Tropics. We are the better off, the better we can lose heat by water evaporation.

Water evaporation from the skin is the most complete when a large part of the skin area is uncovered. The native laborer in the Tropics generally wears but little clothing, often only a breechclout. On the other hand, the white skin can not withstand the direct rays of the sun. Sunburn, *erythema solare*, or even more severe lesions, are produced by the sun's rays, while such injuries rarely occur with the brown skin. The range of the rays which produces this effect is not entirely known, but it is to be presumed that they lie in the violet end of the spectrum and beyond. Now, because of this effect the colored man can expose his body to the tropical sun, but the white man must keep covered. Necessarily, under the same climatic conditions, water evaporation from the skin when uncovered is much more free than that from the same skin covered with clothes. If we further consider that the colored skin

seems to be so arranged as to provide for a greater economy in sweating and water evaporation when exposed to the sun, we must conclude that the colored man, as regards his physical heat regulation in the tropical sunlight, is in a better position than the white man.

The temperature conditions surrounding the parts of the body covered by clothes depend principally on the class of clothing worn.<sup>27</sup> It will be important to learn what proportion of the heat rays are absorbed by the clothes, how freely they permit of water evaporation from the skin and how far free circulation of air is possible within them. The question of the extent to which heat regulation in the Tropics is affected by different kinds of clothing is of great physiologic and hygienic importance, and this problem will be considered in future investigations.

While men, by reason of their superior facilities for evaporating water, are able to counteract the radiated heat from the sun more efficiently than dogs, cats, rabbits, or monkeys, this heat is not without its influence on the human being. The water loss which equalizes the radiated heat is considerable. A man lying quietly in the sun, in one hour lost 280 grams in weight. The water actually lost from the body must have been considerably more, because the sweat absorbed by the clothing is not included in the above figure. The pulse rate of a man sitting quietly in the sun increases on an average about 10 to 12 beats over the number for the same man in the shade. I have proved this by several observations. The quantity of air respired is also increased. An average of a number of observations shows the following:

*Quantity of air respired in liters per minute.*

Number of observations.	Mini- mum.	Maxi- mum.	Aver- age.
22 in shade.....	4.70	5.98	5.28
17 in sun.....	5.83	7.90	6.74

Therefore, the volume of air respired increases 23 per cent, or from 316.8 liters per hour in the shade to 390.4 liters in the sun.

If heat production within the body is very great, as it is during strenuous muscular work, then, even in a temperate climate, the heat-regulating apparatus is not able to diminish the heat by water evaporation as quickly as it is produced, and as a result rises in the body temperature are observed (Zuntz und Schumburg).<sup>28</sup> If at the same time the body is also heated by radiation, the heat accumulated must be greater with a corresponding rise in body temperature.

<sup>27</sup> Zuntz, Löwy, Müller und Caspari, *Höhenklima und Bergwanderungen in ihrer Wirkung auf den Menschen*, Berlin (1906).

<sup>28</sup> Studien zu einer Physiologie des Marsches, Berlin.

This increased body temperature probably accounts for many of the accidents which usually are described as *sun stroke* or *heat stroke*; however, several strokes of this kind, some even fatal, have been reported with but slight rises in temperature. No reasonable explanation of these in relation to the heat rays have been given. I wish to offer one explanation which seems to me quite plausible: Under unfavorable climatic conditions during muscular work, P. Schmidt has observed water losses as great as 1 kilogram per hour. The body can withstand a loss of water in a maximum of 10 per cent of its weight. An acute loss of 3 to 4 kilograms within a few hours, according to our experience with animals (Czerny), necessarily must result in severe disturbances, collapse or even death. It seems quite reasonable to assume that an excessive, continued water evaporation, while avoiding a rise of the body temperature, may lead to collapse, similar to that observed in cholera if the water lost from the body is not replaced.

## SUMMARY.

1. Under climatic conditions, even during the cooler seasons of the year in Manila, animals, such as rabbits and monkeys which by nature have only a limited power of physical heat regulation, or animals the physical heat regulation of which is artificially inhibited (tracheotomized dogs) die if exposed to the sun, the body temperature rising to febrile heights. If the same animals are protected from the rays of the sun, or if the increase of heat due to radiation from the sun is compensated by an increased loss such as would be brought about by a strong wind, then the animals suffer no discomfort. Insolation of the skull alone is without effect if the body temperature is kept within normal limits.

2. The post-mortem findings on the animals dying as a result of insolation show decided hæmorrhagic lesions of the meninges in the brain, and in monkeys, in the heart.

3. In animals without sweat glands the subcutaneous tissues are heated by the radiated heat from the sun to temperatures above those compatible with life.

4. The human skin if exposed to the sun is warmed to about  $3^{\circ}$  to  $4^{\circ}$  above the normal skin temperature ( $32^{\circ}.5$  to  $33^{\circ}.5$ ). An increase, even to the normal body temperature, is prevented by evaporation of sweat. The cooling effect of the sweat secretion causes a fall of the skin temperature even if insolation is continued during longer periods.

5. The brown skin of Malays, while theoretically absorbing more heat in the sun, shows a smaller rise in temperature in the tropical sun than the skin of white men under similar conditions. As an explanation, it is believed that an earlier and better water evaporation by sweat secretion takes place.

6. The air in the human hair, especially in black hair, under the

influence of the tropical sun acquires temperatures far above those compatible with life.

7. It is demonstrated that in the tropical sun a man with a colored skin is in a better position as regards heat regulation than is a man with a white skin.

8. Types of apparatus suitable for testing temperatures thermoelectrically are described.

In concluding, I wish to invite attention to more general biologic questions as regards climate. The monkey, whose home is in the Tropics, withstands the sun less readily than any other animal I have observed, including even the white man. Of course, the monkey does not live in the fields; his home is in the forest, into which only a small proportion of the direct rays of the sun can enter. He instinctively avoids exposing himself to the sun for more than a few minutes. The same is true of the native of the Tropics, if he is left to his own customs. Even if he is otherwise nearly naked, he often wears a large hat-like arrangement which shades not only his head but his body.

Certain features of any climate must always be met. The temperate climate is only suitable for man if he protects his body against it. Our chemical heat regulation would not be sufficient to allow us to withstand the cold of temperate climates without the protection of clothes and houses.

The question of the best way to live in a certain climate will always be to learn how to avoid its injurious effects, or to secure protection against them. No better example than the monkey, which is killed by the tropical sun in from one to two hours, can be found to confirm the above statements.

## ILLUSTRATIONS.

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PLATE I. Hearts of monkeys exposed to the sun.  
II. Brain of monkey exposed to the sun.

### TEXT FIGURES.

- FIG. 1. Diagrams showing connections between galvanometer and thermocouple.  
2. Diagram of a thermocouple used in taking temperatures of the skin.  
3. Second type of apparatus used in temperature experiments.





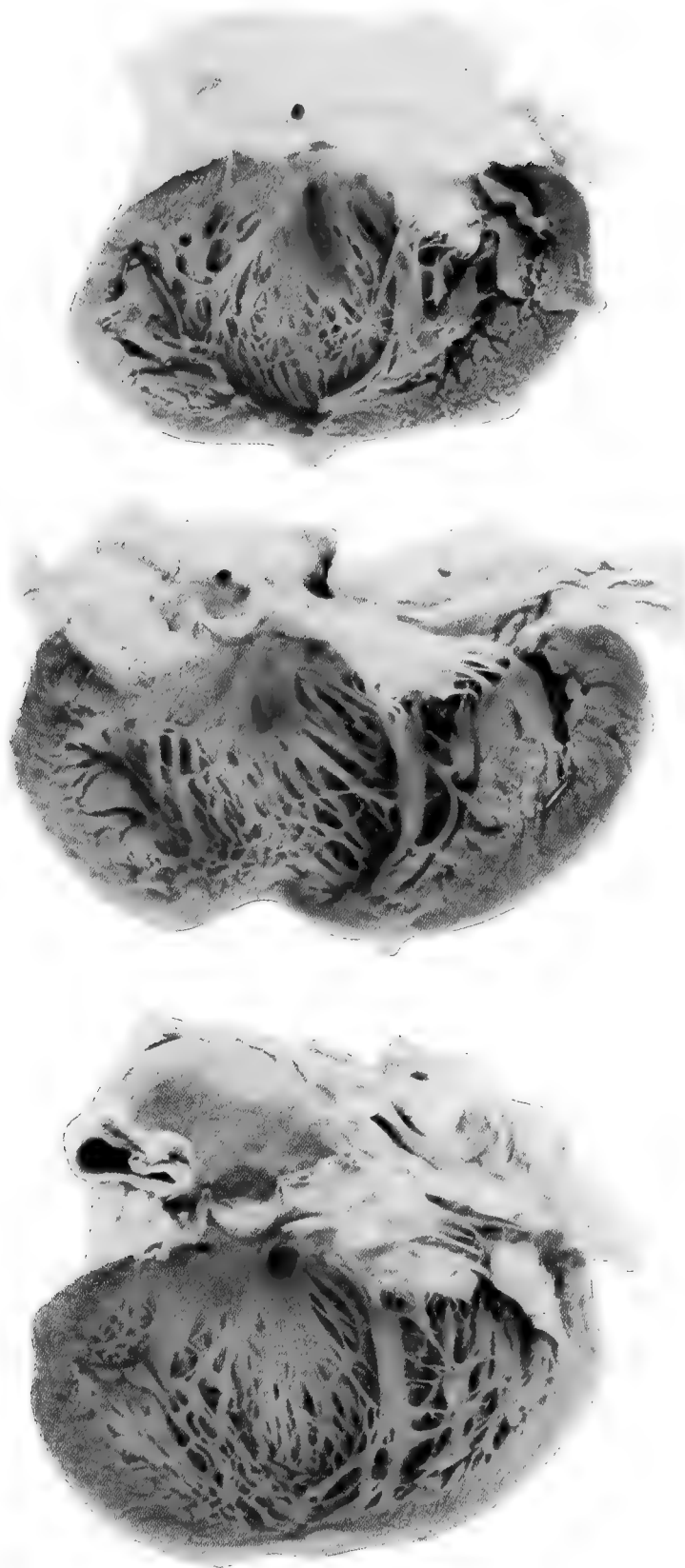


PLATE I.



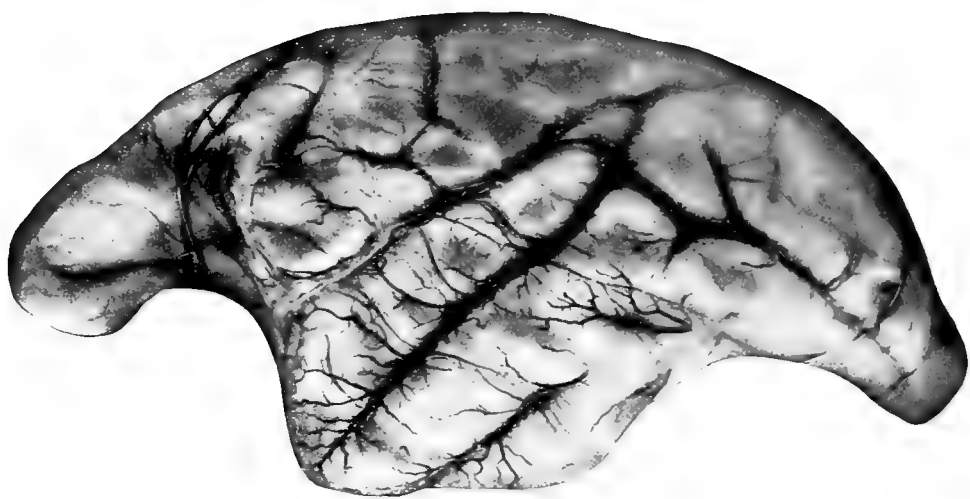


PLATE II.



# THE ERADICATION OF BERIBERI FROM THE PHILIPPINE (NATIVE) SCOUTS BY MEANS OF A SIMPLE CHANGE IN THEIR DIETARY.<sup>1</sup>

By WESTON P. CHAMBERLAIN.<sup>2</sup>

## I. CHANGES IN THE FILIPINO RATION FOR SCOUTS<sup>3</sup> IN THE YEAR 1910.

Influenced by the work of Braddon, Stanton, Fraser and others on the effects of highly milled rice, this Board investigated in 18 Scout companies the incidence of beriberi as related to the diet actually consumed by the men.<sup>4</sup> As a result of the knowledge gained the Board (then consisting of Captains Phalen and Kilbourne) on September 30, 1909, recommended that the following changes be made in the Filipino Scout ration:

1. That the daily amount of rice used per man be limited to 16 ounces instead of the 20 ounces formerly allowed.

<sup>1</sup> Read, with permission of the Chief Surgeon, Philippines Division, before the Philippine Islands Medical Association at Manila, P. I., February 22 to 24, 1911.

<sup>2</sup> Major, Medical Corps, United States Army; President of the Board for the Study of Tropical Diseases as they exist in the Philippine Islands.

<sup>3</sup> The organization known as the "Philippine Scouts" consists of approximately 5,000 Filipino enlisted men serving as infantry. The commissioned officers are Americans. This organization is under the control of and supported by the War Department of the United States and is scattered in small garrisons throughout the Archipelago. The Philippines Constabulary, referred to later, is under the control of the Insular Government and has an enlisted strength of about 4,000 Filipinos. It is much more widely scattered in smaller garrisons than is the Scout organization and it has an entirely different system of rationing its men.

<sup>4</sup> Kilbourne, E. D., Food Salts in Relation to Beriberi. *This Journal, Sec. B* (1910), 5, 127.

2. That Filipino number 2 rice (an undermilled article) be substituted for choice Saigon rice (highly milled.)<sup>5</sup>

3. That 1.6 ounces of beans be added to the ration in place of the 4 ounces of rice not used.

4. That the issue be authorized of canned tomatoes in lieu of an equal quantity of potatoes, but not to exceed 20 per cent of the total issue.

5. That onions be issued on the same terms as tomatoes instead of allowing them to be substituted for the entire quantity of potatoes.

6. That no savings be permitted upon the ration of fresh beef and potatoes or their substitutive articles.

The components of the Philippine ration at the time of these recommendations are shown in the following table:

TABLE I.—*Filipino ration, Army Regulations 1908, paragraph 1220.*

Component articles.	Quantities.	Substitutive articles.	Quantities.
Beef, fresh -----	12 ounces----	{Bacon -----	8 ounces.
		{Canned meat..	8 ounces.
		{Fish, canned..	12 ounces.
		{Fish, fresh ---	12 ounces.
Flour -----	8 ounces----	Hard bread --	8 ounces.
Baking powder, when in field and ovens are not available. -----	0.32 ounce----		
Rice -----	20 ounces----		
Potatoes -----	8 ounces----	Onions -----	8 ounces.
Coffee, roasted and ground -----	1 ounce----		
Sugar -----	2 ounces----		
Vinegar -----	0.08 gill----		
Salt -----	0.64 ounce----		
Pepper, black -----	0.02 ounce----		

It should be explained for the benefit of those not in the military service that such a ration does not indicate exactly what a company eats. "Savings" can be and usually are made on some components of the ration

<sup>5</sup> "Polished rice," "highly milled rice," "scoured rice" and "white rice" have been used by various writers as synonyms. They are contrasted with "undermilled rice," "medium milled rice," "unpolished rice," and "red rice," all four terms indicating that more or less pericarp has been left on the grain. Some rices have red pericarp and others have white. If the red pericarp is all milled off, the grain is then white. Therefore, the use of the term "white rice" to indicate a highly milled article is objectionable because it leads to confusion between milling processes and color of pericarp.

As far as the presence of adherent pericarp is concerned undermilled rice corresponds with the "cured rice" of India (not used in the Philippines) and the "Filipino number 2" rice of the Scout ration prescribed by General Orders, No. 24.

and the money value thereof used to purchase other articles of the ration, or articles not on the ration, for the purpose of adding variety to the company bill of fare; or the money value of the articles saved may be added to the company fund.

The first and third recommendations and indirectly that portion of the sixth recommendation relating to the saving of fresh beef were made effective by the following instructions of the division commander and must have gone into operation at the individual posts between the middle of November, 1909, and the first part of January, 1910.

HEADQUARTERS, PHILIPPINES DIVISION,  
*Manila, November 3, 1909.*

The COMMANDING GENERAL,

*Department of Luzon (Visayas, Mindanao, and Camp Avery), Manila.*

SIR: The division commander directs that the attention of all Scout battalion and company commanders be called to the directions of the Secretary of War, that, with the exception of the meat component of the ration, Scouts will be rationed as largely as possible on native food products; to the recommendation of the Board for the Study of Tropical Diseases, that the amount of rice be reduced from 20 ounces to 16 ounces per ration, and that beans to the extent of 1.6 ounce per ration be used in lieu of rice; to Army regulation 1262, under which native food products not procurable locally can be obtained from the subsistence department as exceptional articles.

In view of the above, company commanders should not draw rice to exceed 16 ounces per ration. Savings should be made as largely as possible on potatoes, onions and coffee, and native products, such as camotes, mongos, squash, ginger root, etc., be purchased.

Very respectfully,

(Signed) J. T. KERR, *Adjutant-General.*

Furthermore, steps were taken by the subsistence department to obtain a Filipino number 2 rice (undermilled) to replace the highly milled or "polished" Saigon rice which was used for the Scouts. None of this undermilled rice, however, went into use until about August (as will be shown below). We consider that the provision of undermilled rice combined with the above instructions of the division commander would have put into effect the most essential features of the Board's original recommendations.

The situation was complicated by the arrival, toward the end of March, 1910, of General Orders, No. 24, War Department, February, 1910. This order greatly altered the Scout dietary. The components of the ration thus prescribed are shown below:

TABLE II.—*Filipino ration, General Orders, No. 24, War Department, 1910.*<sup>a</sup>

Component articles.	Quantities.	Substitutive articles.	Quantities.
Beef, fresh -----	12 ounces---	Bacon -----	8 ounces.
		Canned meat-----	8 ounces.
		Fish, canned -----	12 ounces.
		Fish, fresh -----	12 ounces.
Flour-----	8 ounces---	Hard bread -----	8 ounces.
Baking powder, when in field and ovens are not available.	0.32 ounce---		
Rice, <i>Filipino No. 2</i> -----	16 ounces---	<i>Rice, Saigon</i> (when <i>Filipino</i> <i>No. 2</i> can not be obtained).	
<i>Camotes</i> <sup>a</sup> -----	8 ounces---		
<i>Mongos</i> -----	4 ounces---		
Coffee, roasted and ground-----	0.5 ounce---		
<i>Ginger root</i> -----	0.5 ounce---		
Sugar-----	2 ounces---		
Vinegar -----	0.08 gill---		
Salt-----	0.64 ounce---		
Pepper, black -----	0.02 ounce---		

<sup>a</sup> The *camote* is a vegetable allied to the sweet potato. The *mongo* (*Phaseolus radiatus* Linn.) is allied to the bean. "Filipino No. 2" rice as the term is used in this ration means an undermilled rice.

The Board had no knowledge of this new ration prior to the promulgation of the order in the Philippine Islands. It will be seen, however, that the order carried out in spirit the three most important recommendations of the Board in that an undermilled rice (*Filipino No. 2*) is prescribed in the amount of 16 ounces daily and mongos (equivalent to beans) are added to the ration in lieu of the 4 ounces of rice taken away.

#### DATES ON WHICH THE COMPONENTS OF THE NEW RATION WENT INTO USE.

The subsistence department at once proceeded to obtain mongos and camotes, but in order to use up the large supply of Saigon rice on hand a delay occurred in the issue of the Filipino number 2 rice. In determining the dates on which the Scouts would actually begin to subsist on these new articles one must consider the date the article was delivered to the quartermaster's department in Manila for shipment to posts, the time of sailing of the transports, the time spent on the voyage, the time spent in unloading and the delays (due to rations being drawn

<sup>a</sup> Since July 1, 1910, Scout companies have been authorized to make money savings on the entire ration and purchase therewith such articles as they need, but the purchases must be made from the subsistence department, provided it has the desired articles in stock. This new system does not materially affect the feeding of the Scouts. The money value of the ration at the present time is about 14 cents United States currency.



only three times a month) which would occur after the articles actually reached the commissary officer at the Scout post and which could not average less than five days. All of these factors except the last have been embodied in Table III. From a careful study of all the conditions it is possible to set a date before which none of the articles could have become a part of the diet, and a period during which they must have been gradually going into use.

None of the Filipino number 2 rice could by any possibility have been in use prior to July 15, 1910, and but little could have been issued at any time in July. In August the issue became more general, and probably all Scout companies were supplied by the last of August or first part of September.

The first consignments of mongos and camotes were shipped simultaneously and none left Manila until May 20, 1910. Under the most favorable conditions of unloading and prompt issue one Scout command (three companies) *might* have put mongos and camotes into use as early as May 21, but probably did not. No other Scouts could possibly have been using these camotes and mongos before May 25 even granting that they were issued at once on arrival at the station. About half of the Scouts could not have received any mongos and camotes until well into June. The issue to the last of the posts was not completed till the first part of July.

The first shipments of ginger root occurred at the same time as those of camotes and mongos. In some of the Mindanao posts ginger root was received about ten days sooner than camotes and mongos, but not, however, before the last two or three days of May.

The importance of fixing these dates will be appreciated when the beriberi statistics for 1910 are considered. The details for the shipments are shown in the following table:

TABLE III.

Article of ration.	First received in depot commissary, Manila.	Dates first invoices were turned over to the quartermaster's department for shipment to Scout posts in the Department of—		
		Luzon.	Visayas.	Mindanao.
No. 2 rice.....	July 5, 1910 ..	July 14 to Aug. 23 ..	July 14 to Aug. 3 ...	July 5 <sup>a</sup> to Aug. 5.
Camotes .....	May 20, 1910 ..	May 20 to May 23 <sup>b</sup> ..	May 20 to June 2 <sup>c</sup> ....	June 3 to June 8. <sup>c</sup>
Mongos.....	May 18, 1910 ..	May 19 to May 25 <sup>d</sup> ..	On May 18.....	June 3 to July 7.
Ginger root ...	May 19, 1910 ..	May 20 to June 17 ..	May 20 to June 2 ...	May 19 to July 8.
Time consumed in transit to individual posts.		2 to 16 days; average, 4½.	4 to 11 days; average, 7½.	4 to 18 days; average, 10.

<sup>a</sup> This July 5 shipment reached Cotabato on July 13 and Torrey Barracks and Davao on July 15. Issues to the troops were not to be expected immediately after it arrived.

<sup>b</sup> One post rationed August 17.

<sup>c</sup> One post rationed July 2.

<sup>d</sup> One post rationed June 3.

## THE CHARACTER OF THE RICE SELECTED.

The Filipino number 2 rice selected by the subsistence department was examined as regards its pericarp by this Board and approved. It was a mixed rice, having grains with red pericarp mingled with those having a white pericarp. A large amount of the pericarp had been left on the grain. By analysis made in the office of the Surgeon-General of the Army it was found to contain, nitrogen 1.32 per cent, potash ( $K_2O$ ) 0.223 per cent and phosphoric acid ( $P_2O_5$ ) 0.489 per cent, whereas the polished rice it replaced had contained only 1.08 per cent nitrogen, 0.098 per cent potash and 0.260 per cent phosphoric acid.

The mixed red and white rice was approved for two reasons. First, it was possible to determine at a glance, without staining, whether sufficient pericarp remained on the kernel. Second, it was thought that if this red rice proved unwelcome to the Scouts a change could be made in subsequent contracts to an undermilled *white* rice which, by contrast with the red rice, would then probably prove acceptable, whereas it would undoubtedly have aroused hostility if substituted immediately for the highly polished article the subsistence department has in the past been issuing to the Scouts and which they have come to like because of its snowy appearance when cooked. It is probable that few of the Scouts were used to such a highly polished article prior to their enlistment, and in many sections of the Islands a red, undermilled rice is commonly used. After several years in the military service where they received only the highest grade of polished rice these natives have become spoiled in this respect, and it was to be anticipated that the substitution of an undermilled rice, whether red or white, would be distasteful to them for a time.

The truth of the above reasoning has been demonstrated by the experience of the Philippine Civil Government. At the Culion leper colony the inmates objected to an undermilled red rice, but apparently are satisfied with an equally undermilled rice having white pericarp. The use of undermilled rice has eradicated beriberi from that and other civil institutions in the Philippines, and at this point it may be mentioned that on May 4, 1909, Governor-General Forbes issued Executive Order No. 37, forbidding the use of polished rice in any public institution.

## DISSATISFACTION WITH THE NEW FILIPINO RATION.

For many reasons the new Filipino ration, as ordered by General Orders, No. 24, caused dissatisfaction among the troops and in the subsistence department. The Filipino number 2 rice, in addition to being undermilled, contained many unhusked kernels and much broken grain and dirt and furthermore was thought to become infested with worms and insects more readily than did polished rice. The camotes did not

keep well and neither they nor the mongos could always be obtained in sufficient quantities in the Island markets. Therefore, some had to be imported. The ginger root was not acceptable to the Scout as a partial substitute for coffee. Neither mongos nor camotes met with favor as constant articles of diet.

#### RETURN TO THE OLD FILIPINO RATION.

The dietary problem was still further changed on November 7, 1910, when General Orders, No. 24, prescribing the new Filipino ration, was revoked by a cablegram from Washington. The question of diet therefore reverts to its former status, viz, the old Filipino ration (Table I) with 20 ounces of polished rice as a component. There is, however, so much Filipino number 2 rice on hand in the subsistence depots that its issue and use will continue for several months. Meantime the Board is making efforts to have the ration modified to the extent of forbidding the use of more than 16 ounces of rice daily per man and prescribing a first grade undermilled rice with white pericarp, in place of the highly milled grain which the ration now calls for.

#### LESSON LEARNED FROM USE OF FILIPINO NUMBER 2 RICE.

A very desirable lesson has been learned from the issue of the Filipino number 2 rice. The Board now recognizes that the term Filipino number 2 rice was an unfortunate one for two reasons. First, some samples of commercial Filipino number 2 rice are highly milled or polished; second, this rice is second grade not only in respect to its milling (i. e., pericarp removal) but also as to its husking and screening and probably at times is produced from an inferior quality of *palay* (padi). The original selection by the Board of Filipino number 2 rice as the beriberi preventing type was due to the fact that when our recommendation was made no other kind of undermilled rice could be found in the Manila market and there was much less knowledge of and interest in the subject, on the part of the rice dealers, than is now the case.

What the Board now recommends for the Scouts is a rice of the highest grade and in all respects like the "choice rice" of the subsistence department except that it is "undermilled" (i. e., has much of its pericarp left on). In this connection the use of the word "milling" refers only to the process of decortication carried on (in most mills) between a stone cone and the metal-gauze case within which the stone revolves, and does not have reference to the other processes carried out in the building, such as husking, winnowing, screening and polishing between sheep skin buffers. We also recommend that, for appearance sake only, this rice be prepared from *palay* having a white pericarp.

Such a rice can now be produced in these Islands and the millers state that its keeping qualities should be equal to those of highly milled rice. The Board has recently examined samples of a rice from Siam styled "Asylum No. IV." This is an undermilled rice prepared under the supervision of Doctor Highet, of Bangkok, who states that it has been used for six months in an asylum and found to prevent the development of beriberi. Except for an occasional red grain, the rice is white and has much the larger part of the pericarp remaining on the kernels. There are very few unhusked or badly broken grains. The dealers state that they can furnish in quantity rice conforming to this standard. This rice is found by the Bureau of Science to contain 0.52 per cent of phosphorus pentoxide and this we consider an index of its safety. It appears that rices containing over 0.4 per cent of phosphorus pentoxide will prevent beriberi, and this can be used as an indicator, irrespective of whether or not one accepts the phosphorus theory of beriberi production.

## II. GREAT REDUCTION IN THE BERIBERI ADMISSION RATE IN THE YEAR 1910.

The numerous changes which have occurred in the Scout ration during the year 1910 render necessary a somewhat elaborate analysis of the situation before one can decide to which factors should be ascribed any peculiarity which may be found in the beriberi rate for the period. From the standpoint of scientific dietetic study it is unfortunate that so many alterations were made in such close sequence.

Let us now determine if any peculiarity is manifest in the beriberi admission rate for the year 1910. A glance at the following statistical tables will settle the question by showing an unprecedented decrease in the amount of that disease among the Scouts for the calendar year 1910.

TABLE IV.—*Beriberi statistics for Philippine Scouts, calendar years 1902 to 1910.*

Calendar year.	Mean strength Surgeon-General's Office.	Admissions.		Deaths.		Discharges for disability.	
		Num-ber.	Rate per 1,000.	Num-ber.	Rate per 1,000.	Num-ber.	Rate per 1,000.
1902 -----	4,826	598	123.92	29	6.01	2	0.41
1903 -----	4,789	614	128.21	22	4.59	5	1.04
1904 -----	4,610	334	74.62	7	1.52	6	1.30
1905 -----	4,732	170	35.93	6	1.21	1	0.02
1906 -----	4,759	176	36.98	9	1.79	6	1.19
1907 -----	4,679	115	24.58	6	1.28	3	0.54
1908 -----	5,085	618	121.54	7	1.35	13	2.50
1909 -----	5,369	558	103.93	12	2.17	33	5.96
1910 -----	5,422	50	10.00	2	0.36	3	0.55

TABLE V.—Admissions for beriberi by months, calendar years 1908 to 1910.<sup>1</sup>

Year.	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Total.
1908 -----	14	34	102	23	51	33	55	39	63	59	88	63	624
1909 -----	138	89	96	88	38	24	28	36	7	27	22	11	604
1910 -----	19	8	12	3	4	1	0	2	0	0	0	1	50

From a study of Table IV, it is plain that beriberi was very prevalent during 1902 and 1903 and that there was a *slow and gradual* yearly decrease in its incidence down to 1907, when the total number of admissions had fallen to 115. In 1908 there was a sudden increase to 618 admissions, the largest number recorded in any one year. In 1909 the number of admissions was but little less, 558, while for the year 1910 there were only 50 admissions, a most significant drop when it is considered that all the sanitary conditions were unchanged except the diet. The drop in the death rate and in the discharge rate are equally remarkable.

### III. RELATIONSHIP BETWEEN DECREASE OF BERIBERI AND CHANGES IN DIETARY.

It will be seen in Table V that 39 (or 80 per cent) of the admissions occurring in 1910 appeared in the first three months of the year, a time when the ration changes recommended by the Board had been in effect but a short time, or were just being put into effect. It is important to note that some decrease in admissions began in the last quarter of 1909 and that just prior to that time members of the Board had visited many Scout posts, especially those where the disease was rife, and had investigated the dietary actually in use and advised company commanders to limit the daily consumption of rice and to use liberally the other components of the ration instead of economizing for the purpose of making cash savings. We believe that the effect of the Board's recommendations at the Scout posts visited, followed by the ration changes inaugurated by the division commander and by General Orders, No. 24, has been to diminish the quantity of rice consumed by Scout companies

<sup>1</sup> Table IV, except for the year 1910, is taken from the reports of the Surgeon-General of the Army. Table V is compiled from records in the office of the Chief Surgeon, Philippines Division. The discrepancy between the total admissions in the two tables is due to the fact that in the chief surgeon's record a new admission is recorded if a patient is transferred from one hospital to another, whereas in the Surgeon-General's report one admission is recorded for such a case. The admissions (50) for 1910 should really be compared with the chief surgeon's figures for 1908 and 1909 (624 and 604, respectively). This would make the showing even more favorable than is given in the text. Fractionally it means that the admissions for 1910 were less than one-twelfth of the average for the two preceding years.

and to increase the amount of meat, beans (mongos) and other components used. The harmful influences attributed to polished rice are believed by us to be due not to the presence of any injurious element in such rice, but simply to the absence from it of some substance necessary for proper nutrition. Hence, it becomes evident that a diminution of the quantity of rice consumed and a substitution therefor of suitable articles of food might produce the same results as would be obtained from the use of an undiminished quantity of rice in which the necessary nutritive substance was present in proper amounts. Therefore, favorable results following the carrying out of our recommendations would by no means be in opposition to the polished-rice theory of beriberi even when the good results appeared before the undermilled rice went into use.

UNDERMILLED RICE NOT THE CAUSE OF DECREASE IN BERIBERI ADMISSIONS.

It is obvious on examining Tables III, V, and VI *that undermilled rice could have had nothing to do with the great decrease in beriberi admissions which occurred prior to August 1, 1910*, and it probably could have had nothing to do with the low rate in August. Undermilled rice *may have contributed a share* to the continuance of the good results in September, October, November and December.

INFLUENCE OF MONGOS, CAMOTES, AND GINGER ROOT ON DECREASE OF BERIBERI.

A study of Tables III, V, and VI (together with the remarks above Table III) will show that the marked decrease in the beriberi rate for April and May and probably for June could not have been due to the mongos, camotes, and ginger root added to the ration by General Orders, No. 24. At this writing there are no figures to show how extensively mongos and camotes were used as a result of the division commander's letter of November 3, 1909; so that a beneficial influence from mongos and camotes prior to May, 1910, can not be excluded. For reasons which will not be entered into here the Board does not consider that there is any special virtue in mongos and camotes as compared with beans and Irish potatoes which would enable them to prevent beriberi. There is little doubt that the mongo is a good beriberi-preventing vegetable, but it is not any better than the bean recommended by this Board on September 30, 1910. We do not consider either camotes or potatoes of much value in preventing the disease. The influence of ginger root can be eliminated because of its date of issue as well as for other reasons.

THE REAL CAUSE OF THE ERADICATION OF BERIBERI FROM THE SCOUTS.

From the above discussion the Board concludes that the important beriberi preventing factor in the new Filipino ration prescribed by General Orders, No. 24, was neither mongo, nor camote, nor ginger root, nor undermilled rice, *per se*, but was *the reduction in the quantity of rice consumed and the substitution, in lieu of the rice taken away, of a*

*legumen*, which in this case was mongos but which might equally well have been beans as recommended by the Board on September 20, 1910.

The following table will show graphically the periods over which there was active each one of the five new factors, (a) undermilled rice, (b) camotes, (c) mongos, (d) ginger root, and (e) reduction of rice to 16 ounces and addition of a legumen. The solid part of the lines indicates the period during which the influence was general and the dotted part the period during which the influence was beginning and did not affect all the Scout organizations.

TABLE VI.—*Beriberi admissions by months, calendar year 1910, and influences acting thereon.*

	Jan.	Feb.	Mar.	Apr.	May.	June.	July	Aug.	Sept.	Oct.	Nov.	Dec.
Admissions-----	19	8	12	3	4	1	0	2	0	0	0	10
No. 2 rice (a)-----							.....	—————				
Camotes (b) -----					.....	—————						
Mongos (c) -----					.....	—————						
Ginger root (d) -----					.....	—————						
Reduction and leg- ume (e) -----	..	—————	—————	—————	—————	—————	—————	—————	—————	—————	—————	—————

It is obvious that factor (e), viz, reduction in the amount of rice and addition of a legumen, is the *only one* which has been operative during the whole period of marked decrease in beriberi admissions.

It might be argued, by those favoring the nitrogen starvation theory, that the decrease in beriberi in 1910 was due to an increase in the amount of meat consumed by the Scouts as a result of the letter of the division commander which directed the making of savings as largely as possible on potatoes, onions and coffee. We do not think that an increased meat consumption has been an important factor for the following reasons: (a) The Scout did not as a rule make large savings on his meat component and (b) the meat allowance is so great (12 ounces) that the Scouts could make considerable savings thereon and still have an amount larger than is furnished the soldier of many of the European armies, the French allowing 10.6 ounces of meat, the Russian 7.75 ounces and the Austrian 6.7 ounces. In considering these figures it should be borne in mind that the average weight of a Filipino is about four-fifths that of a European or American.

#### IV. BEARING ON BERIBERI RATE OF FACTORS OTHER THAN DIETETIC.

During the year 1910 we are aware of no changes in the sanitary conditions among the Scouts, other than dietetic, which could account for the lowered incidence of beriberi. There has been no marked decrease during 1910 in the admission rate for other diseases. The

average monthly admissions for all diseases was 420.5 in 1908, 393.9 in 1909 and 341.5 in 1910. Since beriberi was causing an average monthly admission of over 50 in 1908 and 1909, while the average was only 4 in 1910, it is evident that the average monthly admissions for all causes other than beriberi was not materially lower in 1910 than it was in 1909.

That the reduction in beriberi among the Scouts in 1910 is not coincident with a corresponding lessening of beriberi cases in the general population in the Philippines may be inferred from the following table of death rates which was furnished us through the courtesy of the officials of the Bureau of Health:

TABLE VII.—Deaths from beriberi.

Fiscal year.	In Manila.	In 22 provinces (population about 5,000,000).	Total.
1906 -----	406	2,228	2,634
1907 -----	403	1,377	1,777
1908 -----	492	1,180	1,672
1909 -----	924	1,765	2,689
1910 -----	1,002	1,395	2,397
1911 (first half) -----	911	( <sup>a</sup> )	-----

<sup>a</sup> Not obtainable.

It should be noted that the rates in Tables VII are for *fiscal* years while those in Tables IV and V are for calendar years. Also that the rates for Manila, 1911, are only for *half* a fiscal year and correspond to the calendar period of June to December, 1910, a period when the admission rate for the Scouts was practically *nil*. We do not attach much absolute importance to the figures in Table VII because the death rates for the general population of the Philippines, even in Manila, are notoriously unreliable for beriberi as well as for other diseases. We do feel, however, that the rates are, relatively, as reliable for 1910 as for the few years preceding and that therefore any extraordinary reduction in the incidence of beriberi in 1910 would have been mirrored in these figures which show a decided increase rather than a decrease in the death rate for the calendar year 1910 in Manila.

The number of cases of beriberi among the Philippine (native) Constabulary, furnished through the courtesy of Major S. C. Guernsey, are as follows: 1908, 52 cases; 1909, 193 cases; 1910 (11 months), 61 cases.

The occurrence of cases by months for 1910 is shown in Table VIII and compared with admissions for same months among the Scouts.



TABLE VIII.—*Comparison of admissions for beriberi among Scouts and Constabulary.*

	January.	February.	March.	April.	May.	June.	July.	August.	September.	October.	November.	December.
Scouts-----	19	8	12	3	4	1	0	2	0	0	0	1
Constabulary-----	7	14	1	1	7	7	9	4	3	2	6	(?)

The Constabulary consists of approximately 4,000 enlisted men, widely scattered throughout the Archipelago. For some years their beriberi rate has been much less than that for the Scouts, this difference probably being due to the fact that they are differently rationed. The admission rate for 1910 is only one-third that for 1909, but is higher than for 1908. On looking at Table VIII it is obvious that there was no such falling off in the beriberi admission rate among the Constabulary for the last half of 1910 as was seen among the Scouts.

It must be admitted that the very high Scout death rate (2.17 per 1,000) and discharge rate (5.96 per 1,000) for beriberi in the year 1909 may have been to some extent responsible for a low admission rate in 1910 because these two processes, death and discharge for disability, doubtless eliminated many old chronic cases which had kept returning on sick report after apparently having been cured. We do not think, however, that this was the important feature in lowering the admission rate for 1910.

#### V. SUMMARY AND CONCLUSIONS.

##### THE BOARD STILL ADHERES TO THE POLISHED-RICE THEORY OF BERIBERI PRODUCTION.

The real factors in the eradication of beriberi from the Scout organizations have been a reduction in the amount of rice consumed and the addition of a legumen. The result was accomplished without the use of undermilled rice. The Board still favors the polished-rice theory of beriberi production as being the one best supported at the present time by experimental evidence and practical experience in many localities. It is considered that the good results with the Scouts help to support the theory. The Board feels that the adoption of an undermilled grain for the Philippine Scouts will allow rice to be used more freely by these soldiers with less risk of beriberi than would be the case if the polished article were supplied to them. This is a very important point because, as a result of racial taste and custom, a certain number of natives will attempt to subsist mainly on rice no matter how extensive, varied or well balanced may be the diet supplied to them by the subsistence department. If polished rice is being issued to the troops, those men will be

the first to develop beriberi whenever for any reason a period of unfavorable dietetic administration supervenes.

Since rice is the natural and economical diet for the oriental native it follows that the free use of undermilled rice is likely to work in the direction of both efficiency and economy.

CONCLUSIONS.

(1) Beriberi has disappeared from the Philippine (native) Scout organizations during the last half of the year 1910.

(2) There have been no sanitary improvements to account for this except the changes in diet and there has been no corresponding decrease in the admission rate for diseases other than beriberi.

(3) There was no corresponding decrease in the incidence of beriberi in the general Filipino population or in the Philippine (native) Constabulary.

(4) The decrease in admissions for beriberi among the Scouts was clearly marked for four months before the use of undermilled rice began.

(5) The decrease in admissions was well under way before the mongos, camotes and ginger root of the new ration began to be issued.

(6) The decrease in the admissions for beriberi was due either to unknown causes acting coincidentally with a reduction in the amount of rice used and the addition of a legumen, or was due directly to these dietetic changes. As no other reduction in admissions even approaching that of 1910 has occurred since the organization of the Scouts in 1901 we do not believe that the present decrease is due to coincidence.

(7) The facts do not oppose the polished-rice theory of beriberi production. On the contrary, we believe that they support it.

# A CASE OF DYSENTERY CAUSED BY *BALANTIDIUM COLI* WITH COINCIDENT FILARIAL INFARCTION OF THE SPLEEN.<sup>1</sup>

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By FRED B. BOWMAN.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

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The clinical history and protocol of the following case illustrate very well the very serious nature of infection with *Balantidium coli*. In a previous paper<sup>2</sup> I reported two cases and there is a great similarity between one of these and that about to be reported, both in the clinical history and the findings at autopsy.

The case was found during the routine examination of fæces at Bilibid Prison, Manila, and was immediately placed under observation in the hospital. The patient, when admitted to the hospital, complained only of mild diarrhoea. He rapidly recovered without any medicinal treatment, the parasites disappeared from the stool, and he was returned to duty. One month later (August 17) the patient was again admitted to the hospital, complaining of pain in the chest, cough, bloody diarrhoea, and fever. Temperature on entrance, 40°. I was unable to follow the case closely for a few days, but the temperature gradually became lower and he seemed to be improving until August 26, when his temperature again began to rise, the pulse became weak and respiration more rapid. On August 30 I examined him and made the following notes:

The patient is a male Filipino, age 40, with no history of previous illness except occasional attacks of diarrhoea during the past year. He appears to be in almost a collapsed condition and is roused with difficulty and then can not answer questions.

He is hiccupping regularly and coughs occasionally, bringing up large amounts of greenish-white material, greenish flakes, and some blood-stained mucus.

The tongue is heavily coated and the breath foul. The eyes are protruded and the pupils dilated. The face is distorted as if from great pain.

There is some pulsation of the vessels of the neck. The pulse is weak and

<sup>1</sup> Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, Manila, February 24, 1911.

<sup>2</sup> *This Journal*, Sec. B. (1909), 4, 417.

thready, although regular. The apical impulse is normally situated and the heart is not enlarged. Pulse rate, 95 per minute.

Breathing is rapid; vocal fremitus somewhat intensified in the base of the left lung, and this area is also somewhat dull on percussion. In the bases of both lungs and up toward the axillæ, coarse râles may be heard and also an occasional friction rub.

The spleen can not be palpated. The liver is normal in size. The abdomen is slightly prominent and this is particularly apparent in the left flank, where there is distinct bulging. The entire abdomen is tender on palpation, but this is particularly noticeable in the colon area on both sides and in the epigastrium. There is great general muscular weakness. The patient lies for the greater part of the time with the legs flexed.

The bowels move frequently and the motion is accompanied by tenesmus. The stool is very thin and sanguineous. During the past week there has been much blood present, more than at any time during the course of the illness.

Microscopic examination of the fæces shows many balantidia present (30 or 40 in one cover-glass specimen) also much blood and mucus.

*Blood examination.*—The blood is very pale and coagulates slowly. Hæmoglobin, 70 per cent; white blood cells, 4,000. Differential counts show no eosinophilia to be present and the blood picture is practically normal. *Urine*, some albumin and a few casts present.

August 31: The patient is much weaker and can not be roused. Heart very feeble. He is still hiccoughing. The abdomen is very tender, but no other signs of peritonitis are observed.

The patient died on September 1 at 4.45 a. m. Many methods of treatment were used without any definite effect being produced. Enemata of quinine, silver nitrate and thymol were given, also ipecac by mouth in large doses.

Protozoa other than *Balantidium coli* were never found during the course of the disease, although the fæces were examined daily. The autopsy was performed by me four hours after death.

The protocol follows:

*Autopsy.*—The body is that of a well-nourished Filipino. Rigor mortis is present. The pupils are equal and dilated. The superficial glands are not palpable. There is a fair amount of subcutaneous fat and the muscles of the abdomen and chest are fairly well developed and of good color.

On opening the thoracic cavity the sternum is raised with great difficulty because of fibrous adhesions. The *pericardial cavity* contains a fair amount of straw-colored fluid. Some fibrous bands may be seen between the visceral and parietal pericardium toward the apex of the heart. A few "milky patches" occur on the anterior portion of the heart, some having tags of tissue attached to them.

A layer of yellow fat surrounds the heart. The coronary arteries are somewhat hard and tortuous. On cut section, the heart muscle is of good color. The wall of the right ventricle is thickened. The valves of the heart apparently are normal with the exception of the mitral leaves, which are thickened and apparently incompetent.

The *aorta* is thickened near the ventricle and is only slightly elastic.

The lungs, both right and left, are firmly attached throughout to the chest wall by fibrous adhesions and can only be removed by rupturing the lung tissue.

Both lungs are crepitant in parts, less so in the apices than in the bases. On

cut section the lung appears mottled with dark red areas surrounding the bronchioles and from these areas bloody serum may be expressed and from the bronchioles a creamy fluid. No nodules or calcified areas can be found. The bronchial glands are not enlarged.

The *peritoneum* is distinctly thickened and is not glistening. Scattered over the surface are grayish-white patches.

The *spleen* is normal in size. The capsule is thickened and fibrous bands of connective tissue attach the spleen to the colon and posteriorly to the abdominal wall. On passing the hand over the spleen surface numerous nodules may be felt from 1 to 3 centimeters in diameter. These project somewhat from the surface. On section, the pulp is friable and congested. The Malpighian bodies are indistinct. The nodular areas extend into the pulp for a distance approximately the same as their diameter on the surface. When a nodule is sectioned the tissue bulges out and is bright red in color. Fibrous bands extend in different directions through the spleen pulp.

The *mesentery* is greatly thickened. The mesenteric glands are not enlarged but many of them show some injection.

The *liver* is somewhat enlarged and firmly attached to the diaphragm above by fibrous bands, and is adherent below to the gut. Cross section shows a loss of normal structure with areas of congestion scattered here and there.

The *gall bladder* is normal and the duct is patent.

The *pancreas* appears somewhat smaller than normal and is firmly adherent to the adjacent viscera. The capsules of the *kidneys* strip with difficulty. The striations are irregular and the kidney substance pale.

The *stomach* appears to be normal, also the duodenum and small intestine. The *colon* (see Pl. I) in its entirety is one mass of ulcers from which hang tags of necrotic tissue. The description given in the previous report<sup>\*</sup> exactly covers the condition here present. The ulceration in this case is rather more general than in the one reported before, but perforation has not taken place. The ulceration is much more severe near the rectum, it gradually becomes less so toward the cæcum and in general appears very much like an amœbic infection.

The urinary bladder apparently is normal. Scrapings from the intestinal ulcers show numerous *Balantidium coli* but no other animal organisms; those from the nodules in the spleen, from the wall of the urinary bladder, and from areas of pleuritis were negative.

*Anatomic diagnosis.*—Broncho-pneumonia; chronic adhesive pleuritis; chronic adhesive pericarditis; splenic infarction; chronic nephritis; chronic adhesive peritonitis; chronic ulcerative colitis (*Balantidium coli*); perihepatitis; mitral endocarditis; arteriosclerosis.

*Histologic examination.*—The histologic examination of all the tissues will not be given, special reference being made only to those organs which were found interesting pathologically.

*Spleen.*—Appears normal in parts, but other areas show severe hæmorrhage, the sinuses being crowded with blood cells and the normal splenic structure indistinct. Filarial embryos may be seen here and there lying close together in the sinuses in groups of two or three. (See Pl. II, fig. 3.) These are much more numerous near the center of the hæmorrhagic areas, gradually decreasing in numbers until the normal spleen tissue is reached.

*Colon.*—Examination of one of the ulcers of the colon shows some balantidia

\* *Loc. cit.*

lying in the necrotic tissue and a few in the mucosa, the largest number being in the submucosa. Here they are seen in nests in the blood vessels and in the surrounding tissue; and they again may be demonstrated in sections cut through apparently normal portions of the gut at some distance from any ulcer.

#### SUMMARY.

During the past three years I have seen ten cases of infection with *Balantidium coli*, although during the past eight months balantidia have been found in the fæces of 16 patients in Bilibid Prison hospital. Two of the ten cases terminated fatally, but the others have had no symptoms other than an occasional diarrhœa. Even in the severe infections, the diarrhœa was more or less intermittent in character, the parasites being found in the fæces only during these attacks. This phenomenon might be explained in the following manner: The organisms, moving along in the submucosa, become so numerous as sometimes to form "nests" from which low inflammations develop, and which, proceeding to ulceration, cause erosion of the mucosa and set free the balantidia. (See Pl. II, fig. 1.) At this time the organisms are found in the fæces. In some areas the blood-vessels appear practically to be occluded by the number of balantidia present and this fact in itself is sufficient to initiate an inflammatory process by lowering the tissue resistance.

The possibility that the parasite may carry bacteria and thus cause an inflammatory reaction has been suggested. I have invariably found that the cellular infiltration which is present around the organisms situated beneath the unbroken mucosa practically consists of lymphoid cells and a few eosinophiles (Pl. II, figs. 1 and 2), very few polymorphonuclear leucocytes being present. This fact in itself seems to show conclusively that the primary inflammation is not caused by bacteria. However, the necrotic material covering the ulcers is composed largely of leucocytes and there is no doubt that the terminal, acute ulceration begun by *Balantidium coli* in the underlying tissue is due to a great extent to the entrance of intestinal bacteria.

The manner of primary invasion is not determined. It has not been established whether the mucosa must be injured before the parasites can enter or whether they in themselves are capable of piercing the uninjured mucosa. A third possibility is that they liberate a cytolytic ferment which causes the injury. However, once an entrance is gained, multiplication rapidly takes place and it is only a matter of time until the entire colon may be infected.

I have examined many preparations, both fresh and stained and fixed in the tissue, but have never seen any distinct evidence of conjugation taking place between two organisms. The balantidia may be seen in groups and in pairs closely attached, but showing no nuclear cytoplasmic

changes. It often has been observed that flagellates and ciliates tend to group themselves together in fresh specimens. This grouping apparently has no relation to conjugation and probably is due to mechanical action alone.

We know that the organisms multiply by division. In almost any field where they are numerous, either in stained sections from colonic ulcers or in stained fæces, partial or complete division of the nucleus may be seen. Balantidia with central constriction may be found in fresh specimens as may also many very small, elongated young forms which seem to be the result of this division. As yet we have had no success as to cultivation. I have observed balantidia alive forty-eight hours after inoculation on Musgrave and Clegg's amœba medium, and Walker in this laboratory has noted life for one week on the same medium, but the balantidia apparently had not reproduced and those which remained alive were left from the original individuals which had been inoculated.

In view of the fact that Brooks has reported an epidemic of dysentery due to *Balantidium coli* among the apes of the New York Zoölogical Park<sup>4</sup> and Noc F.<sup>5</sup> a natural infection in a monkey (*Macacus cynomolgus* Geoff.) we would expect to be able to produce the disease experimentally in monkeys.

I have attempted to infect monkeys, but have been unsuccessful. Fresh fæces from a case of severe infection were many times injected into the rectum and the monkey suspended by his lower extremities in order that none of the material could be evacuated. Frequent examinations showed no balantidia present.

A colotomy was also performed on another monkey and 20 cubic centimeters of infected fæces were injected into the colon on two occasions. The organism never appeared in the fæces.

Some tissue from an ulcer removed at the autopsy reported in this paper was inserted beneath the mucosa of the colon of a monkey and well sutured in. This operation was done in the hope that in the tissue of the ulcer, resting or encysted forms might occur which would be more resistant to manipulation and conditions incidental to the changing of the host, and which might develop and infect the animal. No balantidia were ever found in the fæces, nor were any symptoms of dysentery noted.

I have never seen anything which could possibly be construed as an encysted *Balantidium coli* in fresh fæces, although many round, vacuolated, nonmotile organisms were found in old specimens. In a short time these organisms became flattened and irregular, and extruded granular degenerative material from the periostome.

<sup>4</sup> N. Y. *Aniv. Bull. Med. Sci.* (1902), January.

<sup>5</sup> *Compt. rend. Soc. biol.* (1908), 64.

## CONCLUSIONS.

1. *Balantidium coli* is a parasite and, although not so common an infecting agent as the amoeba, in individual cases it is more serious in its effects. The prognosis in early cases is bad and in late ones practically hopeless.

2. A search through the literature fails to show a report of splenic infarction due to filarial embryos in an uncomplicated infection. Infarcts of the spleen with numerous filarial embryos present have been reported in a case of Bubonic plague.<sup>6</sup>

Infarctions occur frequently in plague and it is possible that the embryo filariæ in the case cited above were only present coincidently and not the primary cause of the infarction.

<sup>6</sup> Über die Beulenpest in Bombay im Jahre 1897. Albrecht und Ghon: II. Wissenschaftlicher Theil des Berichtes. B. (1898), 237.



## ILLUSTRATIONS.

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### PLATE I.

Photograph of colon, showing severe ulceration caused by *Balantidium coli*.

### PLATE II.

- FIG. 1. Section through apparently normal colon, which microscopically shows two balantidia lying in the submucosa causing cell infiltration which will probably proceed to ulceration of the mucosa.
2. Two balantidia lying in the submucosa. Practically no cell reaction present.
  3. Filarial embryos in spleen pulp, causing infarction.





PLATE I.



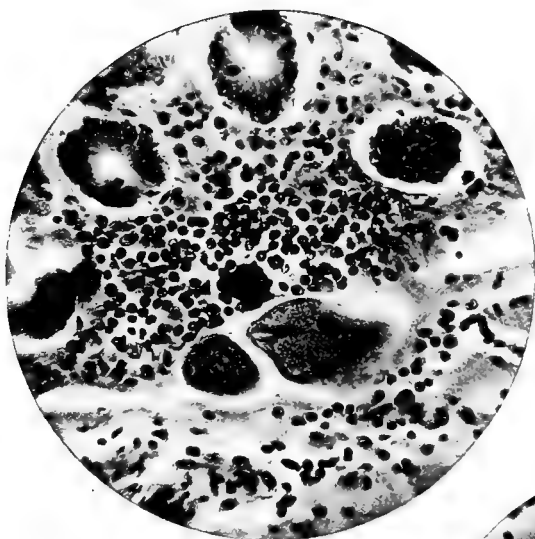


FIG. 1.

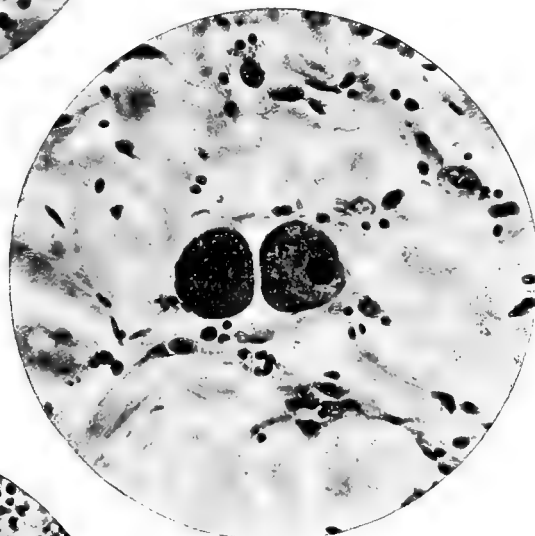


FIG. 2.

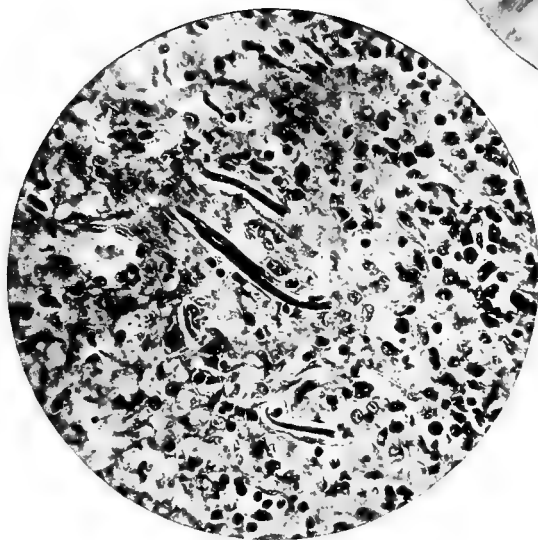


FIG. 3.

PLATE II.



# SOME OBSERVATIONS ON SO-CALLED FLAGELLATES, CILIATES, AND OTHER PROTOZOA ENCOUNTERED IN WATER AND IN HUMAN STOOLS.

(PRELIMINARY REPORT.)

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By E. H. RUEDIGER.

(*From the Serum Section, Biological Laboratory, Bureau of Science, Manila, P. I.*)

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During routine examinations of diarrhoeal stools made a short time ago among members of what may be considered a camping party, flagellates (species undetermined) were encountered frequently, ciliates (species not identified) occasionally, and on two occasions one other protozoön which will briefly be described later on in this paper.

Whenever there is an outbreak of diarrhoea, especially in a camp, the drinking water naturally is one of the first things to receive attention. The drinking water at the place in question was distilled and obtained from a distilling plant about 2 or 3 kilometers from the camp. The water was stored at the distilling plant in a closed, practically air-tight iron tank, and it was delivered in a closed iron tank every morning; it was stored at the camp in large galvanized-iron cans with loose covers, from which the coolers were filled for drinking purposes. In transferring the water from the receiving cans to the coolers a milk pitcher or similar vessel usually was employed and in so doing the hand frequently came in contact with the water, thus making an avenue for contamination; and other chances for infection were numerous. Samples of water from the various places, the distilling plant, the water wagon, the receiving cans, and the water coolers at the camp, were examined as follows.

1. *May 16.*—A sample of 1,000 cubic centimeters of distilled water from the storage tank at the distilling plant and one of the same amount from the water wagon were put into a sterile flask, about 20 cubic centimeters of sterile, melted nutrient agar was added and the whole incubated for three days. Result of microscopic examinations made May 19: No amœbæ, no ciliates, no flagellates.

2. *May 16.*—A sample of 1,000 cubic centimeters of water from the receiving cans at the camp was put into a sterile flask, and the same procedure followed.

Result of microscopic examination made May 19: No amœbæ, no ciliates, but swarming with flagellates.

3. *May 16.*—A sample of 1,000 cubic centimeters of water from the water coolers at the camp was put into a sterile flask, and the method outlined above was followed out. Result of microscopic examination May 19: No amœbæ, no flagellates, but a large number of ciliates were present.

The results obtained with samples 2 and 3 at once attracted my attention. Water from the coolers which previously had been in the receiving cans yielded ciliates and no flagellates, while the water from the receiving cans yielded flagellates, but no ciliates. The appearance of ciliates in water from the coolers is explained readily by assuming that the ciliates were in the coolers when the latter were filled, or that they entered that water in some other manner while the receiving cans had remained free from them. However, the disappearance of the flagellates which were present in the water from the receiving cans and absent from the water in the coolers was not so readily explained and became the subject of some study.

#### EXPERIMENT 1.

*May 21.*—About 10 cubic centimeters of sample 2, containing a large number of flagellates, was put into a sterile test tube and about 10 cubic centimeters of sample 4, containing a large number of ciliates, was added. On microscopic examination many flagellates and ciliates were found. On May 22 microscopic examination showed a large number of ciliates, but no flagellates. On May 23 microscopic examination showed many ciliates, but no flagellates.

#### EXPERIMENT 2.

*May 23.*—A clean bottle of 250 cubic centimeters capacity was nearly filled with water, and about 10 cubic centimeters of melted nutrient agar was added and sterilized. After cooling, a few cubic centimeters of sample 3, rich in flagellates, and a few cubic centimeters of sample 4, rich in ciliates, were added. Microscopic examination made immediately showed a small number of flagellates and a small number of ciliates.

*May 24.*—On microscopic examination, a moderate number of flagellates and a moderate number of ciliates were found.

*May 25.*—Microscopic examination revealed ciliates but no flagellates.

*May 26.*—Many ciliates, but no flagellates.

*May 27.*—A large number of ciliates, but no flagellates.

*May 28.*—Many ciliates but no flagellates.

#### EXPERIMENT 3.

*May 30.*—One large platinum loopful of water rich in flagellates was put into the cavity of a hollowed microscopic slide, three loopfuls of water rich in ciliates were added, and a cover glass placed over the cavity. Microscopic examination made immediately after mixing the two showed a large number of ciliates and a moderate number of flagellates. On examining the mixture two hours later, ciliates only were found, all flagellates having disappeared.

*May 31.*—Microscopic examination made about twenty-four hours after mixing the two showed all ciliates encysted; flagellates were not seen.



## EXPERIMENT 4.

*May 31.*—One large platinum loopful of a culture containing many flagellates was put into the cavity of a hollowed microscopic slide, three loopfuls of a culture containing many ciliates were added and a cover glass placed over the cavity. On examination immediately after mixing, both the ciliates and the flagellates seemed very lively and appeared to attack one another. The motions of the flagellates soon became sluggish, and after about ten minutes ceased entirely. One ciliate which appeared to be about forty times as large as a flagellate, guarded a group of 20 flagellates crowded close together and entirely motionless. The ciliate continually circled around the group of flagellates, and as soon as one of the latter started to move he was attacked by the former which appeared to whip him with its cilia, a few beats of which seemed to render the flagellate motionless. Unfortunately, the observation had to be interrupted and when I returned an hour later all flagellates had disappeared, but the ciliates were actively motile. I was not able to determine in just what manner the flagellates were disposed of, whether devoured by the ciliates or destroyed by lysis. Ciliates, after having disposed of flagellates, contained many large granules which in size and shape corresponded to flagellates and which disappeared within twenty-four hours. Ciliates grown in the absence of flagellates showed no such large granules, on the contrary the organisms were finely granular.

## EXPERIMENT 5.

*June 3.*—One large platinum loopful of a culture of ciliates was put into the cavity of a hollowed microscopic slide, three loopfuls of a culture of flagellates were added and the cavity covered with a cover glass. On examining the mixture immediately after preparation a large number of flagellates and a small number of ciliates were seen. Both were actively motile and appeared to attack one another.

Microscopic examination made an hour later showed the flagellates actively motile and the ciliates sluggishly moving. Microscopic examination ten hours after the specimen was prepared showed the flagellates actively motile and the ciliates encysted.

*June 4.*—Microscopic examination showed the flagellates motile and the ciliates encysted.

## EXPERIMENT 6.

*June 4.*—About 20 cubic centimeters of water were put into a test tube, a small quantity of nutrient agar was added and the mixture then sterilized. After cooling, 1 cubic centimeter of a culture of ciliates and about 10 cubic centimeters of water rich in flagellates were added. Immediately after having been mixed, a moderate number of actively motile flagellates and a small number of actively motile ciliates were noticed under the microscope.

*June 5.*—Microscopic examination showed a large number of flagellates and a small number of sluggishly motile ciliates.

*June 6.*—The flagellates were actively motile and all ciliates were encysted.

*June 7.*—Microscopic examination showed a large number of motile flagellates and a small number of encysted ciliates.

## MULTIPLICATION OF THE CILIATES.

What appears to be the adult ciliate is pear-shaped or egg-shaped, the cilia (their actual number was not determined) are situated at the narrower extremity, and the organism moves in that direction. One nucleus is usually present. The organism increases in size (means for

taking measurements were not at hand), the nucleus divides to form two daughter nuclei, one of which moves toward the narrower, the other toward the broad extremity, the cilia disappear, motility is lost, the organism assumes an oval shape and a transverse constriction appears at the middle. The constriction becomes more and more pronounced, a circle of cilia appears at the proximal end of each daughter cell, the neck continues to narrow, the cilia become motile; finally, division of the cells is complete and each daughter cell, nearly spherical in shape, moves slowly away. As the organism increases in size it assumes a pear-like shape.

Nuclear changes are frequent throughout the process of cell division. The nucleus, large and distinct, suddenly disappears from view, to reappear in a slightly different part of the cell after a few seconds. At times two distinct nuclei are present in a daughter cell, these move toward each other and fuse to form one.

Multiplication of the cells was not observed in the flagellates.

#### CULTIVATION OF THE CILIATES.

The following cultural tests were made in conjunction with bacteria that were present in the water or in the stools. Attempts to grow the ciliates free from bacteria were not successful.

*Nutrient broth.*—When inoculated with material containing ciliates and bacteria, it became heavily clouded and microscopic examination revealed motile ciliates and bacteria.

*Agar-agar.*—A heavy, translucent, whitish, moist streak appeared along the line of inoculation. Microscopic examination showed a large number of motile ciliates and bacteria.

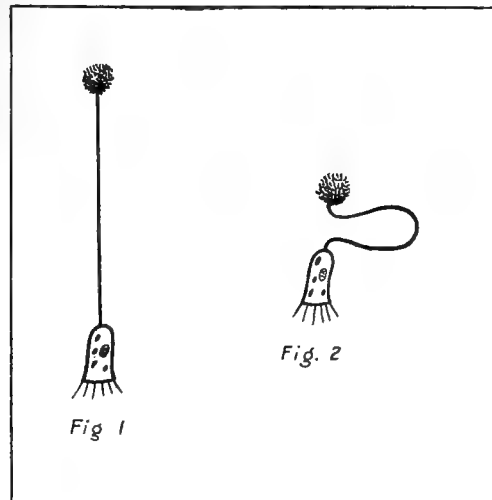
*Lactose-litmus-agar.*—A heavy, translucent, whitish, moist growth appeared along the line of inoculation. Microscopic examination showed many motile ciliates and bacteria.

Attempts to cultivate the flagellates on solid media were unsuccessful.

#### THE OTHER PROTOZOÖN PRESENT IN THE WATER.

The other organism mentioned in the beginning of this paper was twice cultivated from diarrhoeal stools and was always found in cultures made of sewage and from a spring which, during rain, received the surface drainage of several hundred meters of the wagon road. The organism, when seen in cultures made after the method employed in examining water for amœbæ, is bell-shaped. (See fig. 1.) A hair-like line, about five times the length of the organism, arising from the part which corresponds to the top of the bell, extends to a clump of dirt, a cluster of algæ, or any substantial anchorage, where it appears to be fastened. The part which corresponds to the open end of the bell is surrounded by a circle of cilia which are actively motile and set up a whirling motion of

the water surrounding the cell. Apparently there is slight suction into the broad extremity of the cell, which appears to be closed by a membrane. As dirt and bacteria become entangled in the cilia and appear to be sucked against the membrane, the motility of the former ceases and with a quick



jerk the organism assumes the position shown in figure 2. The jerk seems to have freed the cilia and the membrane from dirt, the organism slowly moves back to its former position and the cilia resume their motility.

#### CONCLUSIONS.

1. Flagellates and ciliates seem to antagonize each other. The ciliates, when in sufficient numbers, destroy the flagellates. If the flagellates sufficiently outnumber the ciliates, conditions then are unfavorable for the ciliates and they encyst.

2. The ciliates can without difficulty be cultivated in symbiosis with bacteria on liquid and on solid culture media. Attempts to secure the ciliates in pure culture have failed thus far.

3. The ciliates multiply by transverse division of the cell.

4. Attempts to cultivate the flagellates on solid media were not successful.



## ILLUSTRATIONS.

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### TEXT FIGURES.

FIGS. 1 and 2. A bell-shaped protozoön cultivated from diarrhœal stools.



## REVIEW.

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**The Treatment of Disease. A Manual of Practical Medicine.** By Reynold Webb Wilcox, M. A., M. D., LL. D. Cloth. Pp. viii + 1023. Philadelphia: P. Blakiston's Son & Co., 1911.

This "manual" of over 1,000 pages lacks both the conciseness of a handbook and the fullness and completeness of a system of medicine. The author has attempted to cover too much ground and to discuss diseases beyond his personal knowledge and experience. The value to a general practitioner in the United States of the sections on "Nasha fever," "Japanese river fever," "verruca," etc., seems questionable, while to a practitioner in the Tropics a more complete treatment of these subjects is necessary.

In the nomenclature of diseases the author too often falls into the unfortunate error of referring to the diseases according to the names of the early describers of the conditions, rather than according to their true nomenclature. Thus he describes Brill's Disease, Weil's Disease, Duke's Disease, Friedrich's Disease, Gerlier's Disease, Milroy's Disease, etc.

The use of "Anchylostomiasis" rather than "agchylostomiasis" is not in accordance with the latest revision of the nomenclature of tropical diseases. The arrangement of the subject matter seems logical and clear for the most part.

Of the modernity and accuracy of the subject matter little need be said after noting that typhoid fever, which is now recognized as primarily a septicæmia to be detected by blood cultures and secondarily as an infection of the intestinal lymph nodes, is to be treated, according to the author, with intestinal disinfectants, etc., and then "If the disease is not inhibited the first week of the exhibition of these salts, the problem is complicated by the fact that the infection has become systemic;" and again, in the section on "Beriberi," by noting the statement that "It is, however, quite likely that rice is really the medium through which the germ of this disease operates, because if cured be substituted for uncured rice the disease disappears."

The advantages of this textbook as compared with the more reliable and readable "Practice of Medicine," by Osler, are so few as to make its field of usefulness limited.

D. G.





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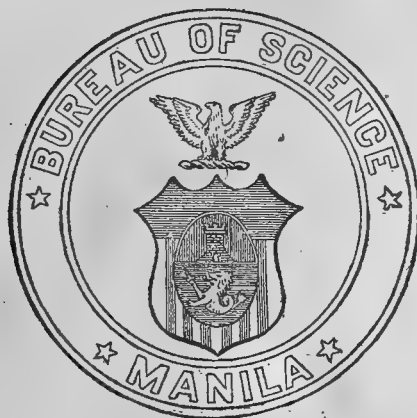
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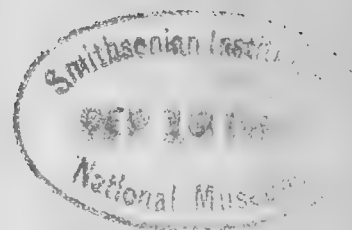
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DAVAINEA MADAGASCARIENSIS (DAVAINE) IN THE  
PHILIPPINE ISLANDS.

By PHILIP E. GARRISON.<sup>1</sup>

The worms studied in the present paper were received from Dr. Vernon L. Andrews, of the department of bacteriology and pathology of the College of Medicine and Surgery, University of the Philippines, who collected them at autopsy from the small intestine of an adult, male Filipino, at the morgue in Manila in March, 1909. Doctor Andrews's specimens are of particular interest because the last finding of *Davainea madagascariensis* (Davaine) was fourteen years ago, and this is only the sixth which has been reported. Infection with this species has been observed only ten times, and the occurrence which forms the subject of this paper marks the Philippines as a new locality in the interesting geographical distribution of this parasite. This new material offers an opportunity for a further study of the anatomical characters of the species.<sup>2</sup>

HISTORY OF THE SPECIES.

In 1867, Dr. Grenet obtained the first specimen from a male child eighteen months old, at Mayotte, Comoro Islands. This child had landed five months before from the Antilles. Later, Dr. Grenet secured a second specimen from a girl two years old, native of Reunion Island, who had been in Mayotte

<sup>1</sup> Passed assistant surgeon, United States Navy, formerly detailed medical zoölogist for the Bureau of Science, Manila.

<sup>2</sup> I am indebted to Dr. Ch. Wardell Stiles for access to a part of the original papers consulted, and to Dr. Brayton H. Ranson for several suggestions regarding the interpretation of certain anatomical characters.

two months. Only about fifteen isolated terminal segments of the worm were secured from the first case. The second specimen consisted apparently of a fairly complete strobila, but was without a head. These specimens were sent to the Directeur des Archives de Medicine and forwarded to Davaine, who, in 1869, described and figured the worms and proposed a new species which he called *Tenia madagascariensis*. These specimens were later deposited in the collection of Blanchard's laboratory (Nos. 108 and 109, Collection Davaine).

In 1873, a second finding of the species was made at the small island of Nosse-Bé, just off the northwest coast of Madagascar. This was not published until 1899 when Blanchard found the specimen in the parasite collection of the Faculty of Medicine of Paris (No. 33, Collection Davaine) bearing the label "Nosse-Bé, November, 1873, passed by a little girl of three years." This specimen was very incomplete, being only 32 millimeters long, but it possessed the head, and Blanchard's paper in 1899 gave the first description and the only published drawing of the head of this species.

In April, 1891, Dr. P. Chevreau announced the finding of four cases of infection with *D. madagascariensis* in children at Port Louis, on Mauritius Island, off the west coast of Madagascar, where, at the instigation of Blanchard, he had made a special search for the parasite. Two of the children were little girls of five years. The sex and age of the other two were not given. The specimen from one of the children, which was sent to Blanchard (Collection R. Blanchard, No. 8) consisted originally of three fragments which in transit were broken into eight, and, according to Blanchard, represented parts of two worms. There was no head. Blanchard gave a brief description of the specimen in 1891.

In the same year (1891) Leuckart reported that he had received from Krabbe a specimen of *Davainea madagascariensis* collected at Bangkok, Siam, from the three-year-old son of a Danish sea captain, living on his father's ship which was plying in Asiatic waters. Later in 1891, Leuckart reported the results of his study of the specimen, which consisted of a single worm about 24 centimeters long, including the head. This material was further studied by Holzberg in 1897.

The fifth and last finding of the species prior to the present one was reported from South America in 1895 by Daniels who obtained two specimens at autopsy from the jejunum of an adult, male aboriginal Indian at Georgetown, British Guiana. The heads were not found and, having only Davaine's original description of *D. madagascariensis* available, Daniels considered his specimens to be specifically distinct and proposed a new species under the name "*Tania demerariensis*?" A part of Daniels's material was sent to Sir Patrick Manson and through him reached Blanchard (Collection R. Blanchard, No. 236) who established its identity with *D. madagascariensis*.

The history of the six findings of *Davainea madagascariensis*, accordingly, extends over a period of forty-two years, and may be summarized as follows:

Grenet, 1867, Comoro Islands, two cases (male child eighteen months old and girl two years old, from the Antilles and from Reunion, respectively), two worms without heads; specimens studied and published with illustrations by Davaine in 1869.

—, 1873, Nosse-Bé Island, one case (three-year-old girl), one immature worm with head; specimen found in Davaine collection, studied and published by Blanchard in 1899 with figure of head.

Chevreau, 1891, Mauritius Island, four cases (two girls five years old, two with age and sex unknown); fragments of two worms without head from one case sent to Blanchard and briefly described the same year.

Krabbe, 1891, Siam, one case (Danish boy three years old); one specimen

complete with head; published by Leuckart in 1891. (Further studied by Holzberg, 1897.)

Daniels, 1895, British Guiana, one case (adult, male native), parts of two worms, no head; published in 1895 as *Tænia demerariensis* with illustrations; part restudied and published by Blanchard in 1899.

Andrews, 1909, Manila, P. I., one case (adult, male Filipino), one complete worm and four nearly complete except the head; deposited, No. 305, in Helminthological Collection, Bureau of Science, Manila, and reported in the present paper.<sup>3</sup>

Three other papers are of special interest in the history of this species.

In 1891 Blanchard and Railliet established the genus *Davainea* in which they placed about twenty-five species, including *D. madagascariensis*.

In 1896 Stiles established *D. proglottina* (Davaine, 1860) of poultry as the type species of the genus *Davainea*.

In 1898 Holzberg published a careful study of the reproductive organs of the genus *Davainea*, Leuckart's specimen of *D. madagascariensis* being among the material examined.

#### IDENTITY OF THE SPECIMEN.

Certain not insignificant differences between the anatomical structure of the Philippine specimen and that described for earlier specimens of *Davainea madagascariensis* will be noted in the course of the following description. These differences were such that it seemed at first that we must be dealing with another species. Further study of the specimen and a careful comparison in detail with the figures and descriptions of other authors have convinced us that while certain differences exist seemingly scarcely consistent with specific identity, an actual comparison of the different specimens will be necessary before the real value of such variations can be ascertained. Such a comparative study should prove most interesting and valuable as well in clearing up certain anatomical differences apparently existing between the several specimens heretofore described. Until the actual comparison of specimens can be made, there is no doubt that Dr. Andrews's specimens found in the Philippines should be placed with those of Grenet, Chevreau, Krabbe, and Daniels in the species *Davainea madagascariensis* (Davaine, 1869) Blanchard and Railliet, 1891.

#### DESCRIPTION OF SPECIMEN.

The specimens received from Dr. Andrews consisted of five worms, one complete with head and gravid segments, the other four evidently nearly complete excepting the head. The five worms were entered in the Helminthological Collection as number 305, A, B, C, D, E. The specimens were killed in an alcoholic solution of bichloride of mercury and preserved in 70 per cent alcohol containing 5 per cent of glycerine.

The size and general characters are as follows:

305 A.—Thirty-nine centimeters long, head present and strobila complete in one piece from head to gravid segments.

305 B.—Twenty-eight + centimeters long, head and neck missing, remainder of worm in one piece from near the neck to gravid segments.

<sup>3</sup> It may be noted that while Davaine named the species after Madagascar, as indicative of the general locality where the first specimens were found, the parasite has never been reported from Madagascar itself.

305 C.—Twenty-nine + centimeters long, head and neck missing, remainder of worm in one piece from near the neck to gravid segments.

305 D.—Twenty-nine + centimeters long, head and neck missing, remainder of worm in one piece from near neck to gravid segments.

305 E.—Four fragments, apparently parts of the same worm; two pieces, 1.5 centimeters and 9 centimeters long, respectively, consisting of rectangular segments; two pieces, 2.5 centimeters and 13 centimeters long, respectively, consisting of terminal, barrel-shaped segments.

The complete specimen with head (305 A) was mounted *in toto*. Specimen 305 D and portions of 305 E were used for sections and digestion. In determining the various anatomical characters, all of the material has been studied.

#### EXTERNAL ANATOMY.

*Head*.—The head and neck unfortunately became badly folded in mounting. The actual breadth of the head as it lies is  $256\ \mu$ . Allowing for the folding, its full breadth appears to be about  $320\ \mu$  but certainly can not exceed  $400\ \mu$ . Blanchard described the head as about  $930\ \mu$  broad by  $510\ \mu$  long.

Leuckart does not give the general dimensions.

The *suckers* in their greatest diameter measure from  $105$  to  $125\ \mu$ , their lumina from  $30$  to  $45\ \mu$ . They are devoid of hooks. In Blanchard's specimen the suckers measured  $465\ \mu$  in diameter with a lumen  $100\ \mu$  in diameter. They also were unarmed. Leuckart does not mention the presence of hooks on the suckers of his specimen.

The *rostellum* is strongly retracted within the head and its contour can not be made out. Imbedded in the head there remain about twelve hooks of the rostellum, of the peculiar "hammer-like" shape of *Davainea*. These hooks measure  $23.5$  to  $25.2\ \mu$  long over all. The long root is rather sharply bent somewhat beyond its middle and measures about  $21\ \mu$  in length and is about  $5.6\ \mu$  broad as it joins the blade. The blade and the short root are continuous in one line, each projecting about  $2.8\ \mu$ , the blade being sharply curved and the short root straight and blunt.

In Blanchard's specimen the rostellum was invaginated, forming an apical sucker  $250\ \mu$  in its transverse diameter and  $145\ \mu$  deep with a deep cup-like depression  $83\ \mu$  in its greatest (transverse) diameter. The hooks were absent, having evidently fallen off. In Leuckart's specimen the rostellum was plump, retracted, about  $100\ \mu$  broad and presented a circular depression at the apex of the head. Around the equator of the rostellum was a ring of about 90 peculiarly shaped hooks, each with a long, slightly curved root measuring  $18\ \mu$ , a short, blunt, posterior root, and a blade about one-eighth the length of the long root, with which it makes an angle of about  $70^\circ$ .

*Neck*.—Because of the folding of the specimen the real breadth of the neck can not be made out with entire satisfaction, but it appears to be about the same as the head, and it is not possible to make out any tendency to the broadening of the neck behind the suckers as described by Blanchard. From behind the suckers the neck gradually grows narrower and reaches a minimum breadth of about  $160\ \mu$  at a distance of about 2 millimeters from the tip of the head. At about this same point the first signs of segmentation are seen and the genital primordia appear shortly after.

Leuckart states that the breadth was "only  $500\ \mu$  just behind the head." Blanchard's specimen measured  $1,240\ \mu$  a short distance behind the head and then decreased to a minimum of  $500\ \mu$ , at which point segments are already defined.

*Segments*.—As stated, segmentation appears at about the minimum breadth of the worm ( $160\ \mu$ ) at a distance from the tip of the head of about 2 milli-



eters. The youngest segments are only about 50  $\mu$  long, there being about 20 in the first millimeter after their appearance. Gradually increasing in length and breadth the segments attain a maximum breadth of 1.5 millimeters about 15 centimeters from the tip of the head and at this place the length of the segments has increased to something less than 1 millimeter, 1 centimeter of the length of the strobila containing from twelve to fifteen segments. Thereafter, the segments increase in length, remaining about the same in breadth, for a distance of from 10 to 12 centimeters, when they are about square. The lengthening then continues, while the breadth shows a tendency to decrease, the segments at the same time beginning to take on the "barrel" shape which becomes more pronounced as we approach the posterior extremity. The terminal gravid segments, which comprise some 10 to 12 centimeters of the length of the strobila, measure about 2 to 2.5 millimeters long by 1 to 1.5 millimeters broad.

The total number of segments in specimen 305 A is about 600.

The younger segments tend to a trapezoidal form, the posterior border being somewhat broader than the anterior and overlapping the anterior extremity of the succeeding segment.

The *genital pores* are not prominent and in the younger segments are situated near the cephalic extremity of the lateral border, later holding a more posterior position, but always well forward of the mid-plane of the segments. They are unilateral with occasional transpositions. Usually the pore will be found on the opposite side in only a single segment, occasionally in two or three, and in one case (specimen 305 D) the pore was found transposed in about 70 consecutive segments.

#### INTERNAL ANATOMY.

*Excretory canals.*—The ventral excretory canals can be followed throughout the length of the strobila, connected at the posterior border of each segment by a transverse canal and attaining maximum diameters of 40 by 20  $\mu$ . The dorsal canal is about half the size of the ventral and can be followed in sections almost throughout the strobila. It is placed in a plane considerably mediad to that of the ventral canal, and both canals are situated a considerable distance to the median side of the *lateral nerve*. The vagina and vas deferens pass between the two canals and behind the lateral nerve in all the segments in which the relative position could be determined.

*Genital organs.*—As indicated above, the segments develop sexually very early in the strobila, the primordia of the genitalia appearing as a dark line in the median field almost with the first appearance of segmentation and while the segments are still only about 160 by 50  $\mu$  and about 2.5 millimeters from the tip of the head.

The *testicles* appear early, when the segment is scarcely 500  $\mu$  broad and 200  $\mu$  long, and before the female genital glands have been clearly differentiated. They are about 50 in number, scattered through the parenchymatous tissue, internal to the excretory canals, and are roughly divided into a dorsal and a ventral layer. The *vas deferens* is extremely long and coiled, extending from the cirrus pouch to about the median line, the coils filling an area from 60 to 120  $\mu$  broad. The *cirrus pouch* is distinctly bottle- or gourd-shaped, situated in the antero-lateral corner of the segment, with its long diameter (neck) directed outward and backward. It measures from 120 to 160  $\mu$  in length by 64 to 100  $\mu$  in breadth. The narrowed neck of the pouch may be nearly straight but more frequently is curved like the neck of a gourd, its concavity being posterior.

After entering the pouch the vas deferens makes two or three irregular coils and enters the *cirrus*, which is about 80  $\mu$  long with a maximum breadth of

12.8  $\mu$ . The *cirrus* is found retracted in most segments, but in a few it is extruded beyond the margin of the segment to a distance of about 25  $\mu$ , the extruded portion being about 8  $\mu$  broad at its base and tapering.

The *vagina* opens immediately posterior to the male orifice, into the common genital *cloaca*, which is rather shallow and projects at the most but a few (15 to 20)  $\mu$  beyond the lateral line of the segment. Close to its outer extremity the vagina presents a well-marked dilatation, the *receptaculum seminis*, which measures 60  $\mu$  long, and 28  $\mu$  broad, being only about one-half the length of the cirrus pouch and reaching not one-half the distance from the lateral border to the ventral excretory canal, whereas, in Krabbe's specimen, according to both Leuckart's description and Holzberg's drawing, the *receptaculum seminis* extended nearly the entire length of the vagina, reaching nearly or quite to the median line of the segment.

From the dilated portion, the *vagina* pursues a course inward and slightly caudad to the median line, where it turns sharply caudad to join with the oviduct, the conjoined tube becoming surrounded by the *shell gland*, and receiving the duct from the *yolk gland* to form the *ootype*. The *uterus*, so far as its structure can be made out in the sexually active segments, appears to consist of a median cavity composed of a number of pouches. The exact arrangement of these pouches and the manner of their gradual extension throughout the segment could not be determined clearly in the sections made, but it seems that the primitive uterine structure gradually extends outward through the parenchymatous tissue of the segment, dividing and subdividing as it progresses, and that small portions, containing one, two, or three eggs each, then become constricted off and lie encased in the parenchyma. The egg-balls form around these pinched-off portions, and their inner, granular zone immediately surrounding the eggs would seem to represent the original uterine structure.

The following description of the *eggs* and *egg-balls* is based upon a study of material digested in a solution of hydrochloric acid and pepsin. Both the egg-balls and the eggs themselves presented a very different and undoubtedly a much more natural appearance when so treated than when dehydrated, stained, cleared, and mounted. In the segments mounted in balsam, either *in toto* or in sections, the balls themselves are shrunken, the outer, lighter zone blends with the surrounding tissue and is not clearly distinguished, the outer shell is marked only by the light area immediately surrounding the embryo and the inner shell is shrunken close around the onchosphere.

In the digested segments the *egg-balls* become separated at what appear to be natural lines of demarcation between their own structure and that of the surrounding parenchyma. The individual egg-balls thus set free are round to ovoid and vary considerably in size, measuring from 200 to nearly 400  $\mu$  in diameter. They present a clear, comparatively structureless outer zone and an inner, denser and more darkly staining area, the latter containing the eggs, which may be one, two, or three in number, most often two. Numerous small (8  $\mu$ ) calcareous corpuscles appear within the inner and outer zones.

If digestion is allowed to proceed further, the egg-balls themselves are broken up and the individual *eggs* are set free. The six-hooked onchosphere is inclosed within two envelopes. The outer envelope is extremely thin and delicate and is easily broken up by slight pressure on the cover glass or removed by a little longer digestion. It tapers to a rather sharp extremity at each end and measures about 120  $\mu$  in length by about 48  $\mu$  in breadth. The inner shell is rather thin and easily distorted and broken, but is considerably thicker and stouter than the outer shell. It is nearly colorless, but has a light yellowish-brown tint.

It is very much elongated, measuring from 50 to 64  $\mu$  long by 19 to 23  $\mu$  broad. One end is bluntly rounded, the other rather more tapering.

The *onchosphere* is circular or nearly so and measures 14 to 15  $\mu$  in diameter. On one side is a slight, blunt, flat-topped eminence bearing the three pairs of nearly straight hooklets, the latter being from 4 to 5  $\mu$  long. Usually the onchosphere lies near the middle of the long diameter of the egg, but it is occasionally displaced to a position near one end.

Other authors who have studied the egg of *Davainea madagascariensis* (Davaine, Leuckart) describe the inner shell as closely enveloping the embryo. Such would be the interpretation in the present case from the appearance of the egg in the mounted specimens, but from a study of the eggs in digested segments it seems quite clear that the inner shell is normally of the form described above and pictured in figure 4.

#### SIGNIFICANCE OF THE PRESENT FINDING.

The first three findings of *D. madagascariensis* in the islands off Madagascar (in 1867, 1873, and 1891) might well have been taken to indicate a possibly narrow range of distribution in that locality, although one of Grenet's cases had come from the Antilles five months previously. Krabbe's case at Bangkok in 1891 at once widened this range greatly and suggested the possibility of a rather extensive distribution. Daniels's case in British Guiana in 1895, as pointed out by Blanchard, opened a new era in the history of the parasite and indicated a general distribution of the species throughout the Tropics. Still, after a lapse of fourteen years, the parasite was not again encountered until Andrews's case in the Philippine Islands completed the belt of distribution around the world and practically gave final proof of the more or less general tropical distribution of the parasite.

From the viewpoint of age distribution it is noteworthy that while six of the eight cases reported in the first four findings of *D. madagascariensis* were young children, the age of the other two not being stated, the last two cases (Daniels's and Andrews's) were adults.

Another interesting point is the apparent relation between the incidence of the infection and maritime surroundings. The first seven cases were insular and all ten have been found at port towns. In addition, two of Chevreau's patients had arrived by ship two months and five months previously, and Krabbe's case, the son of a sea captain, was said to dwell on his father's vessel. The significance of this seeming relationship is problematical. It might mean that the intermediate host is some animal of wide distribution in the Tropics and particularly infesting such situations as ships and docks, for example, the cockroach (*Periplaneta orientalis*) as Blanchard has suggested. On the other hand, further investigation may show the parasite to exist in the interior as well. Heretofore, there has been comparatively little opportunity for investigation in such regions. If this were the case, the apparent relation between the infection and shipping would, in part at least, lose

its significance. We are not aware of the previous occupation of the individual in whom Andrews encountered the parasite, but his residence in Manila could scarcely fail to afford opportunity for infection about the ships and docks of the harbor and river, if such situations are the home of the intermediate host of the cestode. However, the Manila case taken alone would seem to lend itself to almost any hypothesis regarding the source of infection, whether the intermediate host be an insect, mollusk, or fish; and, when taken together with our knowledge of the earlier cases, the fact that Manila is a seaport with a harbor and river full of docks and shipping surely strengthens rather than weakens the apparent relations which have been noted between infection with *D. madagascariensis* and maritime surroundings.

So far as we are aware no one has suggested any more plausible theory regarding the source of infection with this cestode than that of Blanchard, namely, that the intermediate host of the parasite is probably some animal of general tropical distribution particularly infesting ships and docks, and that the cockroach (*Periplaneta orientalis*) would fulfill these conditions. This theory is based in part, of course, upon the analogy presented by the known life cycles of other species of *Davainea*, the larval forms of which live in arthropods or mollusks.

The question as to whether *D. madagascariensis* is normally parasitic in man, or is accidental, having as its normal host some other animal, is naturally suggested by its comparatively rare occurrence in man and by the further fact that species of *Davainea* are so common in birds and so rare in other animals that it is considered distinctly a bird genus among parasites. But in 1899 Blanchard pointed out that while the great majority of species of this genus were parasites of birds, some five species were then known to be parasitic in mammals,<sup>4</sup> namely, three in rodents, one in the ant eater, and one in man, and he unhesitatingly expressed his opinion that *D. madagascariensis* was a normal and not an accidental parasite of man. That the species has now been found in man ten times and has not been reported from any other host during a period of over forty years of active helminthological research would seem to render it reasonably certain that we have in *Davainea madagascariensis* a parasite normal, and perhaps peculiar, to the genus *Homo*.

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<sup>4</sup>Dr. Ransom informs me that one or two of the mammalian species quoted by Blanchard are probably not true *Davaineas*, but that a number of new species of *Davainea* in mammals have since been reported.

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## ILLUSTRATION.

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Explanation of plate. Figures 1 and 2 were drawn from mounted specimens stained with hydrochloric-acid carmine according to the usual method. Figures 3 and 4 were drawn from digested material lightly tinted with carmine.

The drawings were made by Hospital Apprentice L. Avery, United States Navy.

### PLATE I.

- FIG. 1. Sexually mature segment showing the genital organs.  $\times$  about 40. c.=cirrus; c. p.=cirrus pouch; d. c.=dorsal excretory canal; g. p.=genital pore; l. n.=lateral nerve; ov.=ovaries; t.=testicles; trs. c.=transverse excretory canal; v. c.=ventral excretory canal; v. d.=vas deferens; vag.=vagina; y. g.=yolk gland.
2. Terminal gravid segment, showing egg-balls containing one, two, and three eggs.  $\times$  about 35.
3. Egg-ball from digested segment, showing outer and inner layers, calcareous corpuscles, and two eggs with their double envelopes.  $\times$  about 180.
4. Isolated egg from digested egg-ball, showing elongated inner shell containing six-hooked onchosphere.  $\times$  about 600.





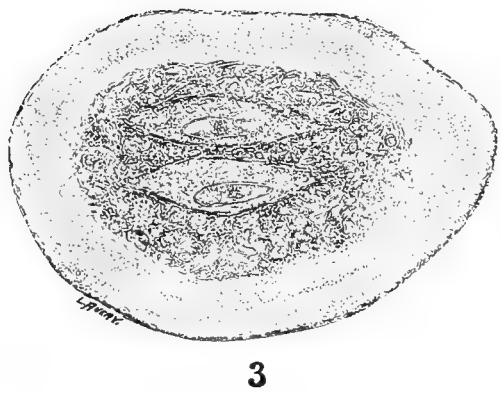
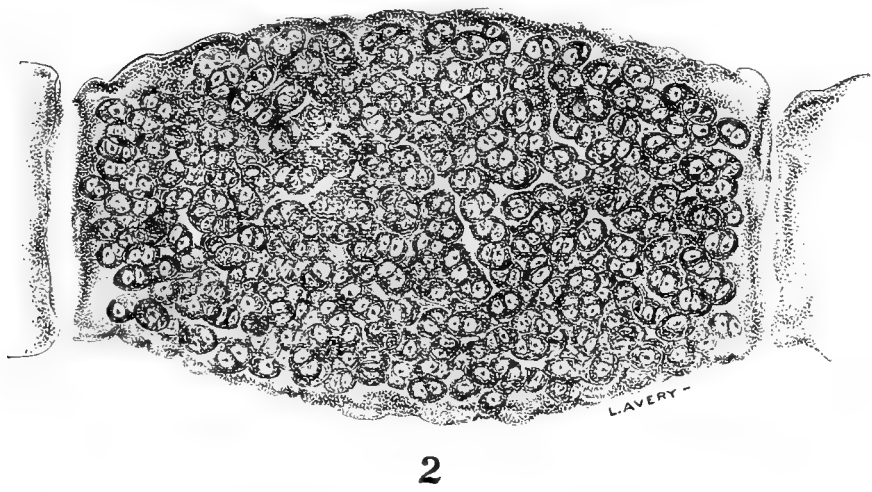
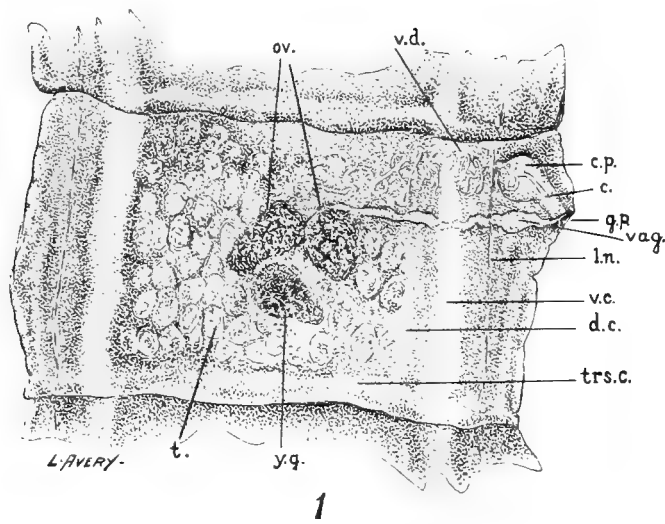


PLATE I.



A STUDY OF THE INFLUENCE OF RICE DIET AND OF IN-  
ANITION ON THE PRODUCTION OF MULTIPLE  
NEURITIS OF FOWLS AND THE BEARING  
THEREOF ON THE ETIOLOGY  
OF BERIBERI.<sup>1</sup>

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By WESTON P. CHAMBERLAIN, HORACE D. BLOOMBERGH, and  
EDWIN D. KILBOURNE.<sup>2</sup>

- I. INTRODUCTION: RELATIONSHIP OF RICE TO BERIBERI AND POLY-  
NEURITIS GALLINARUM.
- II. CHEMICAL COMPOSITION OF PHILIPPINE RICES.
- III. EXPERIMENTS ON FIFTY-SIX FOWLS.
- GROUP A.
- Twenty-nine Fowls Subsisting on Polished Rice.  
*Classes 1, 2, and 3, on polished rice alone.*  
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- GROUP B.
- Thirteen Fowls Subsisting on Undermilled Rice.  
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- GROUP C.
- Four Fowls Subsisting on Unhusked Rice.  
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- Ten Fowls Undergoing Starvation.  
*Classes 13 and 14, on reduced ration of neuritis-preventing rice.*  
*Class 15, on water without any food.*
- IV. GENERAL CONSIDERATION OF MULTIPLE NEURITIS IN STARVED FOWLS.
- V. RELATION OF LOSS OF WEIGHT TO DEVELOPMENT OF POLYNEURITIS GALLINARUM.
- VI. BEARING OF THESE EXPERIMENTS ON THE ETIOLOGY OF BERIBERI.
- VII. CONCLUSIONS DRAWN FROM THE OBSERVATIONS.

<sup>1</sup> Read, by permission of the Chief Surgeon, Philippines Division, at the Eighth Annual Meeting of the Philippine Islands Medical Association, held in Manila, February 23, 1911.

<sup>2</sup> Weston P. Chamberlain and Horace D. Bloombergh, majors, Medical Corps, United States Army; Edwin D. Kilbourne, captain, Medical Corps, United States Army, constituting the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

## I. INTRODUCTION: RELATIONSHIP OF RICE TO BERIBERI AND TO POLYNEURITIS GALLINARUM.

In 1896 Eykman<sup>(1)</sup> conducted feeding experiments with fowls and found that they would develop polyneuritis when fed on polished rice<sup>3</sup> but would not do so when given either *padi* (unhusked rice) or red rice. These experiments were repeated and verified later by Grijns,<sup>(2)</sup> Sakaki,<sup>(3)</sup> and others, and it was shown that the presence of a part of the pericarp or the addition of rice polishings would likewise prevent the disease in fowls.

Polyneuritis of fowls was then thought, and still is believed by many, to be analogous to beriberi of man, and since the fowl is easily experimented with, and is one of the very few animals thus affected, it became the favorite subject for feeding experiments in connection with beriberi.

However, there has always in the minds of many been a doubt whether these two diseases are truly analogous, and some have felt that experiments on man, or on an animal more closely related to man than the fowl, were necessary in order to learn much more about the etiology of beriberi.

Vordeman,<sup>(4)</sup> in 1895-96, in the prisons of Java fed polished and undermilled rice to different groups of men and succeeded in greatly reducing the number of cases of beriberi by the use of the latter variety, and he urged the substitution of red (undermilled) for white (polished) rice in the public institutions of Java.

Braddon<sup>(5)</sup> gave many additional instances of the ill effects of polished rice

<sup>3</sup> The endosperm of rice consists of starch except for a very thin outer portion called the aleurone layer which contains the albuminous material of the seed together with most of the fat. Outside of the aleurone layer is the pericarp or "inner skin" which varies in color from white to nearly black and in the Philippine rices is usually brick-red or yellowish-white. It contains most of the salts in the rice. Outside the pericarp is the husk. Unhusked rice is called by the English *padi* and in the Philippines *palay*.

If a rice have red pericarp and this is completely removed by milling, the resulting highly milled grain is as white as if a kernel with white pericarp had been treated in the same way. "Polished rice," "highly milled rice," "scoured rice," and "white rice" have been used by various writers as synonyms for rice deprived of its pericarp and most of its aleurone layer. The use of the term "white rice" in this sense is objectionable as liable to lead to confusion between milling processes and color of pericarp. The powder produced by grinding off the pericarp and the aleurone layer is called "polishings" in India, and in the Philippines *tiqui-tiqui*. "Undermilled rice," "medium milled rice," "unpolished rice," "Filipino No. 2 rice," and "red rice" are terms which have been applied to rices with considerable pericarp and aleurone layer left adherent to the grain.

As far as the presence of adherent pericarp is concerned undermilled rice corresponds with the "cured rice" of India. Cured rice has been parboiled and then dried before milling, the result being that the pericarp and aleurone layers are less easily removed in the mills. "Cured rice" is not used in the Philippines.

and the beriberi-preventing qualities of the parboiled or "cured" rice, but thought the former carried a toxin generated in it after milling.

Others, having in mind the evidence furnished by previous experiments and epidemics, felt that a privation theory would best account for the occurrence and distribution of beriberi, and experiments were conducted with prisoners, laborers, etc., to prove or disprove the correctness of their deductions.

It remained for Fraser and Stanton<sup>(6)</sup> in 1908-9 to prove beyond all reasonable doubt, in a series of experiments on laborers in the Malay Peninsula, that beriberi could absolutely be prevented by feeding "cured" (parboiled) rice, and that it would occur in the same places and under the same conditions when the men were given polished rice. Since these experiments it has been shown in many countries that the feeding of undermilled rice (which had not been parboiled) has the same beriberi-preventing influence as the use of the parboiled grain and that the beneficial effects of cured rice are due to the adherent pericarp and aleurone layer and not directly to the process of "curing."

As Fraser and Stanton so well put it,<sup>(7)</sup> "The fact that certain white rices when forming the staple of a diet in man produce beriberi rests on quite other testimony than that supplied by experiments on domestic fowls." As a result of their experiments on fowls they concluded<sup>(7)</sup> that while the etiologic connection of polished rice and beriberi was proved by previous experiments on man, the development of multiple neuritis in fowls when fed certain rices is an accurate indicator of the beriberi-producing powers of those rices.

Aron,<sup>(8)</sup> while not going so far, says, "These experiments give us a basis of investigation in order to ascertain the importance of the lack of certain food constituents (such as phosphorus) in producing pathologic changes in the nerves and other tissues."

## II. CHEMICAL COMPOSITION OF PHILIPPINE RICES.

Besides these biologic tests, it is now thought by many<sup>(7)</sup>, <sup>(8)</sup>, <sup>(9)</sup> that the phosphorus content is a good guide in the selection of a beriberi-preventing rice, but, as yet, no absolute standard has been adopted generally.

The officials of the Health Department in Hongkong consider that a rice will not cause beriberi if 0.4 per cent of phosphorus pentoxide is present. As a result of analyses, conducted in the Chemical Laboratory of the Bureau of Science in Manila, Aron considers that a rice is safe when it contains 0.45 per cent of phosphorus pentoxide and unsafe if it contains less than 0.35 per cent. An undermilled rice from Siam, called "Asylum No. IV," and which Dr. Highet has found by practical experience to be capable of preventing beriberi, was shown at the Bureau of Science to contain 0.52 per cent of phosphorus pentoxide.

Whether or not we consider lack of phosphorus to be the cause of beriberi it seems quite generally to be accepted that the amount of phosphorus in a given sample of rice is a reliable *index* of the beriberi-producing power of the grain when used as the principal article of the diet. Samples of the rices used in the succeeding experiments and also

samples of *tiqui-tiqui* were sent to the office of the Surgeon General of the Army for analysis as to the nitrogen, potassium, and phosphorus contents. Doctor Hodge's reports on them are shown in the following table:

TABLE I.—Analyses of rices used in experiments.<sup>4</sup>

Num-ber.	Sample.	Per cent nitrogen.	Per cent potash= K <sub>2</sub> O.	Per cent phos- phoric acid= P <sub>2</sub> O <sub>5</sub> .
1	Choice Saigon rice of Subsistence Department, polished -----	1.08	0.098	0.260
2	Filipino No. 1 rice, polished -----	1.19	0.093	0.255
3	Filipino No. 2 rice, yellowish-white pericarp, undermilled -----	1.20	0.271	0.576
4	Filipino No. 2 rice, red pericarp (Subsistence Department for Scouts), undermilled -----	1.32	0.223	0.489
5	<i>Tiqui-tiqui</i> , white -----	2.18	1.400	5.610
6	<i>Tiqui-tiqui</i> , red -----	1.87	0.973	2.588

It will be seen that numbers 1 and 2 (polished) did not differ very materially from numbers 3 and 4 (undermilled) as regards the nitrogen content but that there was a *great difference in the phosphorus and potassium contents of the polished and unpolished samples*, the latter having twice as much phosphorus pentoxide and two and a half times as much potassium oxide. It is of interest to note that the percentage of salts was lower in the red undermilled rice and the red *tiqui-tiqui* than it was in the white. This indicates a smaller proportion of salts for the red than for the white rice, but whether other analyses indicate such a difference we do not know.

Aron(8) gives the percentage of phosphorus pentoxide for various Philippine rices as follows: Laguna rice, unpolished, 0.557; same, polished, 0.314; "Macan" machinery rice, 0.340; same, native made, 0.455; "Valenciana" highly polished, 0.197; average Manila rice, 0.33. As regards polished and unpolished grades these analyses agree as closely as can be expected with those shown in the above table.

The analyses of our polished rices agree almost exactly with the "white rice" of Fraser and Stanton(7), (17) which contained 0.277 per cent of P<sub>2</sub>O<sub>5</sub>. Our undermilled rice contained more P<sub>2</sub>O<sub>5</sub> than the "parboiled rice" used by Fraser and Stanton, 0.489 and 0.576 per cent for ours as compared with 0.469 for theirs.

To select a rice which has beriberi-preventing qualities, it is not necessary to have a chemical analysis made. Whether the grain be a red or a white variety, a little experience will enable one to determine if sufficient pericarp is left on the kernel. In the case of rices with white pericarp, staining with Gram's iodine solution makes a selection more easy, since the pericarp does not take the stain, remaining grayish white, while the polished grains and the parts of the kernels denuded of pericarp become a deep blue, almost black.

<sup>4</sup>The nitrogen was determined by the Kjeldahl method, the potassium by the Lindo-Gladding.

## III. EXPERIMENTS ON FIFTY-SIX FOWLS.

Our experiments were begun to determine the effects of various Philippine rices on fowls and to use the knowledge thus acquired in the selection of a proper rice for issue to the native troops (Philippine Scouts). As they progressed, several additional experiments were instituted to throw light on some doubtful points observed in the original series, such as the relation of loss of weight and of inanition to multiple neuritis.

The fowls were kept separately in cages 5 feet by 5 feet, made of wire netting and wood; the floor, ceiling, and two sides being of pine boards, tongued and grooved, and the two remaining sides of wire netting with 2-inch meshes. A perch was placed across a corner of each cage about 20 inches from the floor. The cages were arranged in two separate structures each having eight cages, four below and four above. The roof was double with a large ventilating space between the two layers to render the conditions in the upper tier equal to those below. Figure 1 shows them very well. A high board fence around the yard prevented passers by from feeding the fowls. Clean water in enameled cups and a small amount of sterile gravel were kept in each cage. A run, 24 by 38 feet, inclosed by wire netting, adjoined the cages and in it were kept such extra fowls as were not in actual use.

During the course of the experiments six fowls developed infectious conjunctivitis which caused the death of five. From the clinical appearances we concluded that they were suffering from the so-called avian diphtheria which we do not consider to bear any relationship to human diphtheria.<sup>(21)</sup> Two other fowls also had the disease, accompanied by marked nose and throat symptoms. When any signs of this disease appeared, the infected fowls were promptly isolated and not used again for experiment, even if recovery took place. In Tables III and IV those having avian diphtheria are specifically referred to. Great care was taken to eliminate the possibility of this disease being the cause of death or of neuritis in the fowls undergoing experiment.

The sciatic nerves of all fowls dying during the experiments were placed, as soon as possible after death, in a 1 per cent osmic acid solution and subsequently were examined microscopically after being teased out in glycerine. The teasing was done with great care to avoid damaging structures which were really normal and thereby giving an appearance of slight degeneration. For controls the nerves of seventeen healthy chickens were examined by the same method. None of them presented the appearances of degeneration which were found in the fowls that clinically showed symptoms of neuritis.

Our birds were not especially selected as to breed, being the mixed varieties commonly seen in the Philippines, but were carefully inspected for soundness. Only cocks about three-fourths grown were accepted.

The experiments, covering a period of nine months, are given below. They are divided into four groups and fifteen classes, graphically arranged in Tables III and IV.

## GROUP A. TWENTY-NINE FOWLS SUBSISTING ON POLISHED RICE.

In this group of experiments two kinds of polished rice were used; a Philippine Macan rice, purchased in a native shop, and the Saigon variety furnished by the Subsistence Department of the Army, the

latter variety being that supplied the Philippine Scouts (native troops) from the date of their organization in 1901 until about September 1, 1910.

The Saigon rice was very thoroughly milled and polished, scarcely a trace of pericarp remaining on the grains, and in selecting the native polished rice (Filipino number 1) care was taken to obtain a quality similarly free from pericarp. Samples were rejected that showed yellow flakes of pericarp on the dark blue starchy interior, after staining the grains in Gram's iodine solution. The particles of pericarp remaining on the grains of incompletely milled red rice were plainly seen without staining, making easy the detection of unsuitable varieties.

These two kinds of rice, Saigon and Filipino polished, were fed alone in some of the experiments and in others were mixed together and fed in various combinations with salts of potassium and of phosphorus. Phosphorus and potassium were used because by some previous work<sup>(10)</sup> we had shown that these elements were deficient in the diets of the companies of Filipino Scouts having beriberi, and that the deficiency was directly proportionate to the incidence of the disease in those companies.

*Class 1. Fed on Filipino number 1 rice.*—Five fowls were put on a diet consisting of polished native Macan rice (Filipino number 1). By analysis it contained 0.093 per cent of potassium oxide and 0.255 per cent of phosphorus pentoxide. One of these fowls died on the 22d day of avian diphtheria, without signs of neuritis (number 1) and the other four (numbers 2, 3, 4, and 20) developed multiple neuritis after 25 to 33 days (average 29 days) and died on the 30th to 41st day (average 36th day).

None of the fowls seemed to care for this rice after the 3d or 4th day and seldom ate their daily allowance of 118 grams. They declined rapidly in weight, losing an average of 26.3 per cent up to the time of the appearance of the signs of neuritis in the legs and an average of 37.6 per cent to death. Their weight curves are shown on Chart 1.

The signs of multiple neuritis were well marked in these four fowls and, in corroboration, on *post-mortem* microscopic examination their sciatic nerves showed extensive degeneration. Microscopic examination of the nerve of a fowl (number 1) dying of acute respiratory trouble, now thought by us to be avian diphtheria because of our subsequent findings in similar cases, showed no degeneration.

*Class 2. Fed on Saigon polished rice of the Subsistence Department.*—This rice showed on analysis 0.098 per cent of potassium oxide and 0.260 per cent of phosphorus pentoxide. Four fowls were fed on it. Three (numbers 5, 6, and 8) developed multiple neuritis after 25 to 39 days (average 31 days) and two died on the 31st and 36th day respectively (average 33 days). One (number 7) was found dead in his cage after a severe wind and rain storm. He seemed perfectly well the day before and at no time had shown any signs of neuritis.

This class contains two very interesting birds, numbers 5 and 7, and as they are worthy of more than passing notice their histories are given in detail.

Number 5<sup>5</sup> was purchased May 10, 1910, kept under observation for five days

<sup>5</sup> Shown September 5, 1910, to the Manila Medical Society.



in a cage and fed on *palay* (unhusked rice) and kitchen stuff composed of scraps of meat, bread, and vegetables. He was then fed on Saigon polished rice, being allowed 118 grams of rice daily, and, unlike most of the fowls we have used, he ate it all day after day.

He did well until June 23, the 39th day, when he staggered slightly on turning. July 2, the 48th day, he was observed to go down on his knees<sup>6</sup> after exertion. From the 48th to the 90th days he remained about the same, showing his trouble after exercise, but doing very well when not hurried. On August 12, the 90th day, he showed pronounced and typical signs of neuritis, namely, drooping of the wings and inability to keep the legs extended at the knee.

His weight, shown on Chart 1, ran as follows:

Date.	Day.	Grams.	Remarks.
May 16 -----	1st -----	-----	Saigon rice begun.
May 21 -----	6th -----	878	
June 1 -----	17th -----	786	
June 11 -----	27th -----	722	
June 18 -----	34th -----	736	Staggers.
June 23 -----	39th -----	680	
July 2 -----	48th -----	701	
July 9 -----	55th -----	687	
July 16 -----	62d -----	694	Occasionally on knees.
July 23 -----	69th -----	708	
July 30 -----	76th -----	708	
August 6 -----	83d -----	637	
August 12 -----	89th -----	623	Mixed feeding begun.
August 20 -----	97th -----	666	
August 27 -----	104th -----	715	
September 4 -----	112th -----	722	
September 6 -----	114th -----	710	Chloroformed

On the 39th day, when the earliest signs of neuritis appeared, he had lost 22.6 per cent of body weight. From this day to the 76th he remained almost stationary, but from that time on began to lose rapidly until on the 90th day, when the signs of multiple neuritis were marked, he had lost 29.1 per cent.

On the 90th day this fowl (number 5) was given a mixed diet of *palay* and kitchen stuff, in an effort to save him so as to see whether or not spasticity would supervene, as it had in the case of another fowl (number 17) similarly saved from death by mixed diet after the development of neuritis. It had been our experience that fowls went on rapidly to death after acquiring multiple neuritis, rarely living more than five or six days, but in this case (number 5) we were able to save the fowl, and, while his general condition greatly improved from the first, the signs of neuritis grew more marked for several days and then remained stationary until the 114th day, when he was chloroformed.

In addition to the usual leg and wing signs of neuritis there gradually developed a spastic gait. The fowl would stand and walk with knees stiff, teetering forward on the toes, and with the ball of the foot scarcely touching the ground. In an effort to maintain his balance he would take short, quick steps, and seemed to carry the body so far forward that his feet had to hurry to keep up. Figures 2 and 3 are from photographs taken to show the spasticity, but unfortunately do not give a very good idea of it.

<sup>6</sup> In this paper "knees" means the joint formed by the tibio-tarsus and tarso-metatarsus.

We have not been able to find any mention of this spasticity in the literature on the subject. It did not appear in any of our fowls fed on the same rice as number 5 and allowed to go on to death. Evidently it occurs late in the disease. Holst<sup>(11)</sup> speaks of finding some slight degeneration in the white matter of the spinal cord in fowls dead of polyneuritis but does not mention a spasticity of gait observed before death. Microscopic examination of sections of the cord from fowl number 5 showed no degeneration in any of the tracts. The sciatic nerves were extensively degenerated.

Fowl number 7 of this class was remarkable in that he remained well for 89 days on polished rice, showing no sign of neuritis before death, which resulted from exposure in a storm.

In all our experiments with polished rice we have found that those fowls which ate well would remain free from neuritis for much longer periods than the average in whom anorexia with refusal of food appeared early. More will be said on this phase of the subject later in connection with our starvation work in classes 13, 14, and 15. Fowl number 7 ate well from the beginning and always consumed his daily allowance of 118 grams.

His weight, shown on Chart 1, ran as follows:

Date.	Day.	Grams.	Remarks.
May 16 .....	1st .....	.....	Saigon rice begun.
May 21 .....	5th .....	1,162	
June 1 .....	11th .....	1,162	
June 11 .....	21st .....	1,091	
June 18 .....	28th .....	1,071	
June 25 .....	35th .....	1,162	
July 2 .....	42d .....	1,119	
July 9 .....	49th .....	1,119	
July 16 .....	56th .....	1,140	
July 23 .....	63d .....	1,091	
July 30 .....	70th .....	1,098	
August 6 .....	77th .....	1,048	
August 12 .....	83d .....	1,020	
			Found dead.

Microscopic examination of the sciatic nerves showed slight degenerative changes.

The characteristic attitude in polyneuritis gallinarum is shown in figures 4, 5, 6, 7, and 8, which are reproduced from photographs of fowls numbers 6 and 8 of this class.

*Class 3. Fed on 118 grams of polished rice, given by force when necessary.*—In view of the fact that most of the fowls soon tired of polished rice, ate only a small part of their daily allowance, and went rapidly to neuritis and death, we decided to study a series of four which were given polished rice, feeding the fowls 118 grams daily, by force when it was not eaten voluntarily. This amount, 118 grams, was selected because the birds that ate well and remained nearly stationary in weight consumed about that quantity.

The polished rice used was the Saigon grain supplied by the Subsistence Department, and was fed raw and dry. When necessary to use force it was pushed into the crop with the end of the little finger.

It is doubtful if this maneuver was of any use. The bird's appetite was probably a good indication of their ability to digest and assimilate polished rice, and an excess was probably not used.

Of the four fowls thus fed, three (numbers 45, 48, and 49) ate but little voluntarily, speedily lost in weight, and developed multiple neuritis in 27 to 31 days (average 29.6 days) and two of them died on the 42d and 63d day respectively. After showing well-marked signs of neuritis they were given *palay* and kitchen stuff without avail in two cases, which soon thereafter died. One (number 48) was saved by the mixed feeding and, one and one-half months later, had practically recovered the use of his legs and wings. He showed no spasticity at any time. When he had nearly recovered from the neuritis he was turned loose.

The fourth (number 40) differed from the others in that *he ate his full daily allowance and weighed more at the end than at the commencement of the experiment. He did not show any signs of nerve involvement.* He was released on the 81st day of the experiment.

The weight curves of the fowls forcibly fed are shown on Chart 2. It will be seen that the fowl remaining well (number 40) gradually regained the 11.1 per cent of his original weight, which he had lost during the first month.

#### POLISHED RICE COMBINED WITH VARIOUS SALTS.

In an attempt to explain the etiologic connection between polished rice and beriberi, the kinds and quantities of inorganic and organic salts present have received a large share of attention. Schauman and others(8), (9) believe that beriberi results from phosphorus privation. Some(12) have suggested poisoning by, or a lack of, other salts, inorganic and organic, and others have thought that too little of certain proteids or enzymes may be etiologic factors.

After investigating the dietaries of the native troop (Philippine Scouts), the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippines found that the amounts of phosphorus and potassium consumed were deficient in the companies having beriberi, and varied inversely with the incidence of the disease. In our former report on this subject(10) the companies were divided into three classes, as follows:

TABLE II.—Average number of grams consumed per man per day.

Class.	P <sub>2</sub> O <sub>5</sub> .	KCl.
1. Having many cases.....	3.3474	1.0600
2. Having a few scattered cases.....	3.9399	1.1905
3. Having no cases.....	4.6279	1.6517

The amounts of P<sub>2</sub>O<sub>5</sub> average 3.3474 grams in the bad companies, 3.9399 in those slightly affected, and 4.6279 in the companies for the prisoners having no beriberi; a difference of 1.2805 grams between the worst and best averages.

The amounts of potassium chloride average 1.06 grams in the worst, 1.1905 in the medium, and 1.6517 grams in the best organization, a difference of 0.5917 gram between the worst and the best.

These amounts of potassium chloride do not run exactly parallel to the phosphorus content of the three groups, there being a greater relative difference in the amounts of the former. The increase of the best over the worst was 56.76 per cent in the potassium chloride, but only 38.22 per cent in phosphorus pentoxide.

In a set of experiments with fowls we added salts of potassium and phosphoric acid to the diets of polished rice, as follows:

Class 4. Polished rice + 0.05 gram KCl daily.

Class 5. Polished rice + 0.03 gram  $\text{H}_3\text{PO}_4$  daily.

Class 6. Polished rice + 0.06 gram  $\text{H}_3\text{PO}_4$  daily.

Class 7. Polished rice + 0.05 gram KCl and 0.03 grams  $\text{H}_3\text{PO}_4$  daily.

Class 8. Polished rice + 0.03 gram  $\text{H}_3\text{PO}_4$  substituted later by 0.05 grams KCl daily.

In determining the amounts of the salts to be fed, the quantities found to be consumed by the Scouts from the organizations having no beriberi were reduced to correspond to the average weight of the fowls and a small amount added to provide a safe margin. Of course, we have nothing to show the requirements of fowls and they may differ considerably from the human.

The different salts were administered in solutions of such strength that one cubic centimeter of each contained the required dose.

In these experiments with polished rice combined with various salts, we made no attempt to use organic phosphorus in the form of phytic acid or phytin (calcium-magnesium salt of phytic acid) because, first, it was not convenient to obtain these substances and, second, the experiments recently conducted by Aron<sup>(8)</sup> and Kajiura and Rosenheim<sup>(20)</sup> indicated to our minds that no beneficial results were likely to be obtained from their use. This opinion has just been confirmed by the experiments of Fraser and Stanton,<sup>(22)</sup> who found that phytin would not prevent neuritis.

*Class 4. Fed on polished rice + 0.05 gram potassium chloride daily.*—Four fowls were used and all developed multiple neuritis in 22 to 38 days (average 30.5 days) and died on the 29th to 44th day (average 37.5 days).

The weight curves of these fowls (numbers 21, 22, 23, and 24) are shown on Chart 3. The average loss of body weight to the time of the appearance of neuritis was 28.0 per cent and to death 43.8 per cent.

It will be obvious, on glancing at the steep descent of these curves and on considering the time intervening between the commencement of the experiment and the occurrence of neuritis and death, that the administration of potassium chloride was of no avail, the "incubation period" and length of life being practically the same as for fowls fed on polished rice alone.

*Class 5. Fed on polished rice + 0.03 gram phosphoric acid daily.*—Three fowls were put on this diet, and all died after developing typical neuritis. The leg signs appeared after 22 to 27 days (average 23 days) and death occurred on the 27th to 34th (average 30.3 days).

Their weight curves are shown on Chart 3 as numbers 25, 26, and 28. An average loss of 28.2 per cent occurred to the appearance of signs of neuritis and 40.3 per cent of death.

'Nothing worthy of special mention was noted among these fowls except that they developed multiple neuritis and died in a shorter period than those on polished rice alone.

*Class 6. Fed on polished rice + 0.06 gram phosphoric acid daily.*—After observing the shortness of the "incubation period" and the rapidity with which death supervened in the fowls of the preceding class, fed on polished rice combined with 0.03 gram phosphoric acid and to throw some light, if possible, on the reason for this, a set of three fowls was fed the same kind of rice with a daily addition of double the amount of phosphoric acid or 0.06 gram.

Of these three fowls two developed typical leg signs, one (number 60) on the 27th day and one (number 59) on the 31st day (average 29th day).

Instead of allowing them to go on to death we fed them *palay* and kitchen stuff on the 30th and 34th days respectively and, as in the case of fowl number 5, greatly improved their general condition without in any way lessening the signs of multiple neuritis. Both of them also developed spasticity like that observed in number 5 and described in connection with that fowl.

These two fowls were eventually chloroformed. The sciatic nerves showed marked degenerative changes. No evidences of degeneration were found in the tracts of the spinal cords.

Their weight curves, Chart 4, resemble those of fowls fed on polished rice alone. An average loss of 25.2 per cent occurred to the appearance of signs of neuritis and of 30.2 per cent to the end of the experiment, that is to the beginning of mixed feeding.

The fowls of this class kept well nearly a week longer than those on the same rice with one-half the amount of phosphoric acid, but probably this was a mere coincidence, for they fared no better than those of classes 1 and 2 fed only polished rice. The third fowls of this class (number 61) died of avian diphtheria, the lesions being in the nose. Nothing abnormal was found in the sciatic nerves.

*Class 7. Fed on polished rice + 0.03 gram phosphoric acid and 0.05 gram potassium chloride daily.*—In this class the same rice was used as in classes 5 and 6 and the solutions of the two salts were given at different times during the day.

Of the five fowls, three (numbers 29, 31, and 32) developed multiple neuritis in from 21 to 28 days (average 25.3 days) and died on the 25th to 34th day (average 30th day).

The reduction in weight to the appearance of signs of neuritis averaged 32.4 per cent and to death 40.9 per cent.

Two of the birds (numbers 30 and 37) contracted infectious conjunctivitis and died, without signs of neuritis, one on the 4th day and the other on the 24th day of the experiment.

*Class 8. Fed on polished rice + 0.03 gram phosphoric acid for 34 days and 0.05 gram potassium chloride for 91 days.*—One fowl (number 27) was fed in a manner like those of class 5 for 34 days and then, through accident, the acid was replaced by 0.05 gram potassium chloride. It was kept on polished rice and these salts for 125 days, and then weighed but little less than at the commencement of the experiment, and was apparently as vigorous and well as when first placed in his cage.

We do not ascribe his continued good health to the salts but to the fact that he liked polished rice and greedily devoured all that was given him. Only a

few of our fowls have voluntarily eaten freely of this rice and these have been able, by so doing, to maintain their body weight and defer or altogether prevent the development of multiple neuritis.

Number 27 weighed 1,098 grams at the beginning of the experiment and after 125 days weighed 998 grams. A loss of about 15 per cent occurred in the 34 days during which he received phosphoric acid with his rice, and a steady gain took place after the substitution of the solution of potassium chloride; whether or not merely coincidental we are unable to say.

The average time to neuritis of the fowls of all the groups receiving phosphoric acid was 25.3 days as compared with 29.8 days, the corresponding time for those on polished rice alone, and similarly the fowls on phosphoric acid died in an average time of 30.2 days as against 34.7 days when fed polished rice alone.

Food.	Average time to neuritis.	Average time to death.
	Days.	Days.
Polished rice alone-----	29.8	34.7
Polished rice+phosphoric acid-----	25.3	30.2

The difference in favor of polished rice alone is small and may have been due to idiosyncracies of the fowls, or to other factors. *The table shows that the administration of this form of inorganic phosphorus is of no avail in preventing neuritis*, for, if such were the case, the fowls receiving it should have remained well much longer than those fed on polished rice alone, whereas they became sick on an average of  $4\frac{1}{2}$  days sooner.

#### GROUP B. THIRTEEN FOWLS SUBSISTING ON UNDERMILLED RICE.

Two kinds of undermilled rice were used, a Filipino "Macan" rice having a yellowish-white pericarp, and a native mixed rice with about one red grain to every four of the yellow grains. Both kinds were only partially milled, more than half the surface of the grains being covered with pericarp. The second or mixed variety is that now supplied, on the recommendation of this Board, to the Philippine Scouts.

Three classes of experiments were made, first (class 9), those on the first variety of undermilled rice; second (class 10), those on the second; and third (class 11), those on the first plus 0.36 gram sodium chloride daily.

*Class 9. Fed on undermilled rice having a yellowish-white pericarp.*—The rice had 0.271 per cent of potassium oxide and 0.576 per cent of phosphorus pentoxide. Four fowls remained well on this diet for 79 days. None showed the slightest signs of neuritis or other sickness and were in good condition when taken out of the cages. (Numbers 9, 10, 11, and 12.)

Three of the four gained in weight from 4.2 to 17.9 per cent (average 9.4 per cent) while the remaining one lost 17.2 per cent.

*Class 10. Fed on undermilled rice having a red pericarp.*—The rice used in this experiment was that supplied by the Subsistence Department of the Army to the native troops (Philippine Scouts). It contained 0.223 per cent of potassium oxide and 0.489 per cent of phosphorus pentoxide.

Three out of four fowls have remained in perfect health on this diet for an average time of 129.6 days. (Numbers 38, 39, and 47.) The fourth (number 46) acquired infectious conjunctivitis and died, without signs of neuritis, on the 26th day.

The three healthy birds gained in weight from 22.8 per cent to 37.3 per cent (average 29.2 per cent) while subsisting solely on this unpolished rice.

*Class 11. Fed on undermilled rice (yellowish-white) + 0.36 gram sodium chloride daily.*—Bunge in 1894(13) called attention to the relationship of the potassium and sodium salts of the food to each other, maintaining that an excess of potassium carbonate when ingested will react with sodium chloride forming sodium carbonate and potassium chloride which are soluble and are eliminated in the urine, thereby depriving the system of needed elements.

Loeb(14) has shown the necessity for a balance between the sodium, calcium and potassium ions, and that the calcium and potassium ions counteract the effects of the sodium ions in the blood. When marine animals were placed in a pure solution of sodium chloride of the same concentration as sea water, their muscular contractility was lost. Small amounts of calcium and potassium ions antagonized the poisonous effects of the sodium ions.

Le Dantec(15) in the course of experimental work with fowls noticed that the multiple neuritis produced when they were fed on polished rice was seldom (2 cases in 60) accompanied by the œdema which is so frequently observed in the beriberi of man. Desiring to produce this œdema he injected a solution of sodium chloride into the pectoral muscles and killed the birds in every case. He found that it also had the same effect when injected into starving fowls. He made no mention of having administered the salt to fowls not in a cachectic state.

As stated before when describing our experiments with polished rice and various salts, we previously found(10) that the dietaries of the Scout companies having beriberi were deficient in potassium and phosphorus. We also found that the Scouts were rather heavy salt eaters and suggested that this habit may have had an etiologic connection with beriberi by abstracting needed potassium ions.

In class 11 we fed five of our fowls a rice proved by previous experiments (class 9) to prevent neuritis, and in addition gave a daily dose of 0.36 gram of sodium chloride in solution, the amount being decided upon in a similar manner to the determination of the amounts of potassium and phosphorus used in classes 4, 5, 6, 7, and 8. On the 55th day the amount of sodium chloride was increased to 0.72 gram daily.

Four of the five birds continued well, remained stationary or slightly gained in weight, and after an average time of 113.2 days, showed no signs of neuritis. (Numbers 33, 35, 36, and 58.) One fowl (number 34), after nearly two months of apparent health, acquired infectious conjunctivitis and died on the 61st day with a loss of 26.5 per cent of body weight.

*The administration of sodium chloride in either dose, 0.36 or 0.72 gram, seemed to have no effect on these fowls,* but it must be remembered that they were strong animals, receiving a neuritis-preventing rice, were in fine condition, and not cachectic like those of Le Dantec.

## GROUP C. FOUR FOWLS SUBSISTING ON UNHUSKED RICE.

*Class 12. Fed on palay or padi.*—Although unhusked rice has been proved by numerous experiments outside of the Philippines to prevent polyneuritis galinarum, we undertook these tests with the native Macan unhusked rice to see whether or not it possessed the same qualities as the *padi* of other countries and to control the experiments of classes 1, 2, and 9 which were going on simultaneously.

Eighty-one grams of unhusked rice, called *palay* in the native Tagalog dialect, were fed daily to each of four fowls and all remained well to the end of the experiment, 79 days, and showed no abnormal signs. (Numbers 13, 14, 15, and 16.)

A loss of 17.9 per cent and 18.9 per cent of body weight occurred in two of the birds and a gain of 0.6 per cent and 5.6 per cent in the others.

## GROUP D. TEN FOWLS UNDERGOING STARVATION.

As our experiments progressed we noticed that the development of neuritis was invariably accompanied by a considerable loss of weight. In no case did a fowl acquire the disease while gaining or while remaining stationary in weight, indeed, a reduction of 21 per cent or more, except in the cases of fowls numbers 2 and 20, seemed a necessary accompaniment of neuritis. In consequence we decided to feed some fowls reduced amounts of a neuritis-preventing rice and to give others water alone, with the purpose of producing, if possible, a neuritis as a result of partial or complete starvation. That this was accomplished is shown by the following experiments.

*Class 13. Fed on undermilled rice with yellowish-white pericarp. Fifty-two grams (one-half usual allowance) daily for 43 days; followed by 26 grams for 47 days and 13 grams for 25 days.*—One fowl (number 18) was fed 52 grams daily of the neuritis-preventing rice used in class 9, this amount being one-half the daily allowance given the fowls in that class, all of which remained healthy.

With this amount he was able to almost maintain his original weight, losing only a small amount in 43 days. The quantity of rice given was then reduced to 26 grams and from that time a considerable loss of weight occurred, but to hasten the result this was further reduced to 13 grams on the 90th day.

The fowl continued in good condition, except for general weakness which began to be evident about the 90th day, until the 107th day when weakness was particularly manifest in the legs. On the 115th day he was unable to rise, whether from neuritis or general weakness we were unable to say. To determine if possible the condition of his nerves he was then given *palay* and kitchen stuff and rapidly improved except in the legs. He became strong enough to stand, ate well and seemed bright and interested in his surroundings, but had the typical gait and leg signs of neuritis, which became more marked during the two or three days following resumption of mixed diet. He died suddenly on the 122d day. His characteristic attitude is well shown in the pictures, figures 9 and 10.

On microscopic examination his sciatic nerves showed slight degenerative changes.

When signs of neuritis were unmistakable he had lost 46.6 per cent of body weight; at death he had lost 49.4 per cent. His weight curve is shown on Chart 5 as number 18.



*Class 14. Fed on undermilled rice with yellowish-white pericarp, 26 grams (one-fourth usual allowance).—*Fowl number 19<sup>7</sup> was given a ration of 26 grams of the same undermilled rice as was used in classes 9, 11, and 13, and this amount, one-fourth that fed in class 9, was continued unchanged throughout the experiment.

A steady and progressive reduction of weight followed accompanied by increasing weakness. His weight curve shown on Chart 5 as number 19, ran as follows:

Date.	Day.	Grams.	Remarks.
July 14 -----	1st -----	842	One-fourth allowance begun.
July 16 -----	3d -----	821	
July 22 -----	9th -----	765	
July 23 -----	10th -----	751	
July 26 -----	13th -----	736	
July 30 -----	17th -----	694	
August 3 -----	21st -----	659	
August 6 -----	24th -----	595	Died.
August 14 -----	32d -----	538	

On August 11, the 29th day, he seemed disinclined to move, two days later showed well marked early signs of neuritis, and on the following day died. In this case no attempt to save by mixed feeding was made.

A loss of 34.7 per cent to the time of signs of neuritis and 39.5 per cent to death occurred.

The sciatic nerves were extensively degenerated.

*Class 15. Water only.*—In a previous publication(16) we reported a case of typical multiple neuritis in a fowl that had been given water, but no food, and stated that the same experiments would be continued with a larger number of birds. In all we experimented with 8 fowls and *unmistakably produced the disease in three*. Two others very probably had the disease, but we were unable to save them by mixed feeding so could not obtain a clear clinical picture because the signs of neuritis were obscured by those of general weakness. *However, the nerves of these two fowls showed degeneration.*

The histories of these 8 fowls follow and are given somewhat in detail.

Fowl number 17 was purchased May 10, 1910, and kept in a cage on mixed diet, consisting of *palay*, undermilled rice and kitchen stuff, until July 14, when all food was stopped. After July 14, he was allowed only water.

The first signs of trouble were noted on July 26, the 13th day of his fast. He had difficulty in jumping to his perch. On the 21st day he could not get up to it at all. When not disturbed he would stand with head close to the body and eyes closed, but was not observed sitting on his knees. On the 23d day he stood as above and with his knees very straight. When made to walk he showed a tendency to teeter forward. He was evidently very weak and we were unable to feel certain whether his condition was due to pure weakness or to something else. It was feared he would die within 24 hours if he were not

<sup>7</sup>This fowl was reported in a paper read before the Manila Medical Society September 5, 1910, and published in the September *Bull. Manila Med. Soc.* (1910).

fed, consequently we determined to resume feeding with a neuritis-preventing food in the hope that we could save him and make sure that the leg signs were not due solely to weakness. This we accomplished. August 6, the day following the resumption of food, *the signs of neuritis were greatly increased and left no doubt as to the nature of his trouble.* The characteristic attitude is well shown in the figures 11 and 12.

During the following days, in which *palay*, undermilled native rice, and kitchen stuff were fed, *the leg and wing signs became worse*, but his general condition improved rapidly. He became bright-eyed, interested in his surroundings, and gained in weight. His appetite needed no stimulation. The peculiar spasticity he had exhibited at the end of the starvation period increased until walking was performed on his toes, with knees almost straight. An effort to photograph and show the spastic gait was only partially successful. During the last week of his life this fowl partially regained the use of his right leg.

On the 55th day he was chloroformed and the sciatic nerves and spinal cord removed for microscopic examination. The sciatic nerves showed extensive degeneration. No areas of degeneration were found in cross sections of the cord.

His weight, shown on Chart 5, ran as follows:

Date.	Day.	Grams.	Remarks.
July 14 .....	1st .....	991	Starvation begun.
July 16 .....	3d .....	921	
July 22 .....	9th .....	786	
July 23 .....	10th .....	772	
July 26 .....	13th .....	722	
July 30 .....	17th .....	687	
August 3 .....	21st .....	595	
August 5 .....	23d .....	Mixed feeding begun.	
August 14 .....	32d .....	687	
August 20 .....	38th .....	715	
August 27 .....	45th .....	708	
September 4 .....	53d .....	744	
September 6 .....	55th .....	730	Chloroformed.

His loss of weight to the appearance of signs of neuritis was 27.2 per cent and at the end of the starvation period had increased to 40.0 per cent.

Fowl number 41 was put on water alone September 10, 1910. Nothing of importance was noted until September 13 when he became sick with avian diphtheria and died of this infection 5 days later, September 18.

His loss of weight amounted to 39.4 per cent.

Microscopic examination of his nerves showed slight degeneration. No clinical signs of multiple neuritis were observed before death.

Fowl number 42. The water diet was instituted September 10 and was followed by a steady and rapid reduction of weight and muscular strength. On September 26, the 16th day, he was very weak, could not stand, and, when prodded, would not move his legs or wings. Although the general weakness was great we were of the opinion that there was probably, in addition, a peripheral nerve involvement. It was thought that he was not too far gone to revive with mixed feeding and a diet consisting of *palay* and kitchen stuff was then instituted, but without favorable result, for he was found dead in the cage the next morning, the 18th day.

His weight ran as follows:

Date.	Day.	Grams.	Remarks.
September 10 -----	1st -----	963	Starvation begun.
September 18 -----	9th -----	835	
September 24 -----	15th -----	602	
September 26 -----	17th -----	524	Mixed feeding begun.
September 27 -----	18th -----	524	Found dead.

A reduction of 45.6 per cent had occurred when the mixed diet was begun and it is probable that starvation in the case of this fowl was carried too far.

Microscopic examination showed some degeneration of the sciatic nerves.

Fowl number 43 died suddenly on the 14th day of the experiment without having shown any signs of neuritis. The day before his death he showed some general weakness and could not jump up onto his perch, but, on the whole, was in fair condition and we did not anticipate his early demise.

A reduction of 37.6 per cent in weight was observed in his case.

The sciatic nerves were not degenerated.

Fowl number 44. Starvation was begun September 10, water only being allowed. On September 26, the 17th day, he lay on the floor of the cage most of the time; when prodded he would stand and walk a short distance. The gait was that of early neuritis and we had no doubt of its existence. Our belief was corroborated by the *finding of extensive degeneration* upon microscopic examination of the nerves after death, which occurred September 27, the 19th day of the experiment and one day after mixed feeding was begun.

His weight ran as follows:

Date.	Day.	Grams.	Remarks.
September 10 -----	1st -----	970	Starvation begun.
September 18 -----	9th -----	807	
September 24 -----	15th -----	616	
September 26 -----	17th -----	582	Mixed feeding begun.
September 27 -----	18th -----	531	Died.

A loss of 40.0 per cent to the appearance of signs of neuritis, and of 45.3 per cent to death was noted.

No doubt we were unable to save this fowl because inanition was allowed to progress too far.

Fowl number 54. Little need be said of this fowl, for his death occurred suddenly, through an accident, while apparently doing well.

On the 11th day of his fast he seemed in good condition except for some weakness, but the following morning he was found dead with his head and one leg through a small hole in the bottom of the cage. During this time a loss in body weight of 29.8 per cent had occurred.

No degeneration was seen in his sciatic nerves.

Fowl number 55 was kept in one of the cages and fed a mixed diet of *palay* and kitchen stuff for three weeks and then, October 21, given water but no food. Like the other starved fowls he lost rapidly in weight and became progressively weaker until November 5, the 16th day, when feeding with *palay* and kitchen stuff was resumed. On that day he was very weak and lay on his side on the floor

with his eyes closed the greater part of the time. When prodded with a stick he could be made to stand for a very short time. The comb and wattles were deeply cyanosed and his whole appearance was that of a fowl very near to death.

When the grains of *palay* were put before him he would greedily devour them. From that time he improved in general condition, but like number 17 showed more marked signs of neuritis during the succeeding days; unlike that fowl, he did not show spasticity. At this stage pictures were taken which show the usual positions assumed by fowls with the disease. (Figures 13 and 14.) After 9 days of this mixed diet his gait had improved somewhat, but not more so than that of several fowls similarly saved from death after they had developed marked signs of neuritis when fed on polished rice.

He was chloroformed on November 16, the 27th day, and the sciatic nerve removed for microscopic examination; it showed degeneration.

His weight, shown on Chart 5, ran as follows:

Date.	Day.	Grams.	Remarks.
October 21.....	1st.....	963	Starvation begun.
October 30.....	10th.....	892	
November 5.....	16th.....	700	Mixed feeding begun.
November 12.....	23d.....	729	
November 16.....	27th.....	800	Chloroformed.

On the 16th day, when signs of neuritis appeared and the mixed feeding was begun, he had lost 27.4 per cent of his body weight.

Fowl number 56. The clinical history of this bird much resembles that of number 42.

October 21 starvation, except for water, was begun and continued until November 1, the 12th day, when a mixed diet of *palay* and kitchen stuff was given. This fowl declined in weight very rapidly and although starved only 12 days had then lost 44.6 per cent. He died on November 2, the 13th day, after one day of mixed diet. The appearance of this bird was similar to that of number 42; while the signs of nerve involvement seemed present, the general weakness was so great that we could not be positive on this point. However, on microscopic examination the sciatic nerves proved to be moderately degenerated.

#### SUMMARY OF STARVATION EXPERIMENTS.

Two fowls (numbers 18 and 19) were fed reduced quantities of a neuritis-preventing, undermilled rice and both developed multiple neuritis. Eight fowls allowed nothing but water gave three positive cases (numbers 17, 44, and 55), two doubtful (numbers 42 and 56), and three negative ones (numbers 41, 43, and 54).

#### IV. GENERAL CONSIDERATION OF MULTIPLE NEURITIS IN STARVED FOWLS.

Eykman<sup>(1)</sup> did not find polyneuritis in chickens fed on such small quantities of undermilled rice that they died from starvation. Sakaki<sup>(3)</sup> also stated that the weakness in starvation progressed to death without any staggering or other signs of neuritis. Holst<sup>(11)</sup> in speaking of Eykman's nonobservance of polyneuritis in chickens starved on small amounts of undermilled rice, says, "Nor have I found any polyneuritis myself, experimenting in a similar way with pigeons." Likewise Fraser and Stanton<sup>(17)</sup> say in this connection, "Fowls

receiving nothing but water do not develop polyneuritis, while fowls receiving only polished rice and water do."

The only statement to the contrary, we have found in the literature, is that made in the discussion of the beriberi papers<sup>(18)</sup> by Dr. Gorosaku Shibayama, delegate from His Imperial Japanese Majesty's Government to the meeting of the Far Eastern Association of Tropical Medicine, held at Manila, March 5, 1910. He said, "Polyneuritis accompanies general cachexia and inanition in fowls, whereas beriberi, especially the acute, pernicious form, generally attacks well-nourished muscular men."

This statement agrees exactly with the findings in our starvation experiments, and we believe the reason the evidences of neuritis were overlooked by other workers is that *they appear very shortly before death and are obscured by the signs of general weakness*. It is not an easy matter to resume feeding at exactly the proper moment to save the animal and leave the neuritis well developed.

#### V. RELATION OF LOSS OF WEIGHT TO DEVELOPMENT OF POLYNEURITIS GALLINARUM.

The amount an animal can lose and still live varies somewhat with the individual. Withington,<sup>(19)</sup> in discussing starvation, refers to the following:

Chossat stated that the total proportional weight loss of an animal dying of inanition was 40 per cent of the initial weight. But further experiments have shown that a fat animal may lose 50 per cent of its weight, while a lean one can lose only 35 per cent. Young animals in a growing stage have been observed to lose only 30 per cent before they succumbed.

\* \* \* \* \*

The ingestion of water, then, while postponing the fatal result of a fast, produces no important change in the mode of death from that which occurs in simple inanition.

Le Dantec says that in polyneuritis of fowls, when fed on polished rice, the loss of weight is progressive and death occurs when the animals have lost about one-third of their body weight.

Our two fowls, numbers 18 and 19, fed on reduced amounts of un-dermilled rice, lost an average of 40.6 per cent to the end of the experiment, which was death in the case of number 19, and rescue by resuming full diet in the case of the other, number 18.

Those which developed easily recognized signs of multiple neuritis while being given only water, numbers 17, 44, and 55, lost on an average 31.5 per cent up to the time of the appearance of the disease and 37.5 per cent to the end of the starvation period when feeding was resumed. *The losses in this class correspond very closely with those of classes 1, 2, and 3 in which the fowls developed the disease on polished rice alone* and where the decrease in weight averaged 31.6 per cent to the appearance of signs of neuritis and 39.9 per cent to the end of the experiment, which was death in the case of eight and salvation by mixed feeding in two out of the ten fowls.

One can not avoid wondering if the real cause of multiple neuritis in fowls fed on polished rice is not general inanition rather than the lack of any one element in the rice. LeDantec<sup>(15)</sup> says "Fowls nourished on white rice die of inanition and not of beriberi." A similar view is expressed by Breaudat<sup>(23)</sup> who states that animals so nourished die of inanition with symptoms which are similar to those of beriberi. However, he thinks, that intoxication plays a part in the fatal result.

*In further support of the idea that the multiple neuritis of fowls subsisting on polished rice is due to inanition is the evidence supplied by those fowls that seemed to relish polished rice and ate their full daily allowance.* As stated before, nearly all the birds fed on polished rice lost their appetite early in the experiment and would eat little or none of this grain, but a few were exceptions to the rule, notably numbers 5, 7, and 40, and *they remained well for long periods of time.* We are unable to reconcile our findings with the statement of Maurer<sup>(12)</sup> that those fowls which eat polished rice in the largest amounts are the first to become paralytic and that by feeding small amounts of the rice the sickness may be postponed for a long time.

As shown in Table IV, out of the entire 56 fowls experimented with 27 developed neuritis, the average loss of weight up to the appearance of symptoms being 30.9 per cent. In every case but 2 (numbers 2 and 20) a loss greater than 21 per cent occurred before the symptoms developed. Of the 16 fowls which remained well throughout the experiments, only 5 lost weight at all and not one of these five decreased as much as 19 per cent. (Numbers 9, 14, 16, 27, and 33.) Only one fowl (number 40) gained when fed on polished rice and he was well at the end of 80 days when the experiment was concluded.

#### VI. BEARING OF THESE EXPERIMENTS ON THE ETIOLOGY OF BERIBERI.

As stated before, our original object in conducting these experiments was not to prove or disprove the identity of multiple neuritis in fowls and beriberi in man, but to test the neuritis-producing qualities, when fed to fowls, of certain native and imported rices and to use the information thus acquired as an aid in selecting the variety of grain and the degree of milling best suited for the Filipino troops. Nevertheless, as the work progressed, certain points of dissimilarity between beriberi and polyneuritis gallinarum became apparent and it may not be inappropriate to mention them here.

Fowls are especially susceptible to neuritis and get the disease under circumstances which have no effect on the nerves of some other animals. Monkeys, when fed on a diet of boiled, polished rice and water, remained well, although the experiments continued for more than three months. They had lost in weight and become weak, but did not show signs of

neuritis at any time. We can find in the literature no mention of neuritis in man having developed as a result of inanition among the professional "fasters" or among groups of men who were starving.

It would seem that the peripheral nerves of fowls are less resistant to degenerative influences than those of mammals and are among the first tissues to suffer when the animals are starved or given a deficient or ill-balanced diet. Our experience bears out the statement of Shibayama that polyneuritis of fowls occurs in cachectic animals, while beriberi is prone to appear among men previously well nourished.

Another point of difference is that œdema has been very rarely seen in fowls with neuritis<sup>(15)</sup> while it is common in beriberi in man. None of our fowls suffering from neuritis showed any œdema.

Therefore, we are inclined to join forces with those writers who consider that polyneuritis gallinarum and beriberi are not identical but we are fully in accord with Fraser and Stanton in their statements, (a) that its capacity for producing polyneuritis in fowls is an *accurate indicator* of the beriberi-producing quality of a rice and (b) that a low phosphorous content is a *reliable index* of the dangerous character of the grain. However, we have found that in neuritis-producing rice and in beriberi-producing dietaries the potassium is even more reduced than the phosphorus. The comparison between the two elements in rices is shown above in Table I. The diminution in phosphorus as compared with potassium in beriberi-producing diets was treated of in a former communication from the Board<sup>(10)</sup> and is referred to above in the discussion on polished rice combined with various salts (Table II). The latest work of Fraser and Stanton<sup>(22)</sup> seems to indicate that much the greater part (85 per cent) of the phosphorus in rice polishings is of no value in preventing polyneuritis of fowls. It now remains to be shown whether the real neuritis-preventing factor in polishings is the small per cent of phosphorus not yet accounted for, or the potassium, or some other element.

*The inference from the foregoing is that neuritis in fowls and beriberi in man is just as likely to be due to deficiency in salts of potassium as to deficiency in salts of phosphoric acid.* The results of our starvation experiments suggested that, as far as fowls are concerned, it might be a *deficiency of both phosphorus and potassium* which led to nerve deterioration. The experiments in classes 4, 5, 6, 7, and 8 indicated that adding to polished rice either phosphorus or potassium, or both elements, in two of their *common inorganic forms*, did not render the grain any safer as an exclusive article of diet for fowls. We are about to undertake another series of experiments combining with polished rice other mineral salts, such as potassium carbonate, potassium citrate; potassium phosphate, and magnesium phosphate.

## VII. CONCLUSIONS DRAWN FROM THE OBSERVATIONS.

1. Fowls develop multiple neuritis when fed exclusively on polished rice, whether Filipino Number 1 or Saigon choice rice is used.
2. Forcibly feeding polished rice to such fowls as have no appetite for it will not prevent the occurrence of neuritis.
3. Those fowls that voluntarily eat heartily of polished rice are able thereby to maintain their body weight and to defer or to prevent the development of multiple neuritis.
4. The administration of certain inorganic salts of phosphorus and of potassium, either alone or combined, to fowls subsisting on polished rice neither prevented multiple neuritis nor deferred its onset.
5. Fowls fed unhusked rice, *palay*, do not acquire multiple neuritis.
6. Fowls fed undermilled (unpolished) rice do not acquire the disease.
7. Whether the undermilled rice has a red or a yellowish-white pericarp is immaterial.
8. Fowls fed on undermilled rice combined with large amounts of sodium chloride do not develop multiple neuritis.
9. Fowls from which all food is withheld and only water allowed, develop multiple neuritis in some cases.
10. Fowls starved on reduced amounts of a neuritis-preventing undermilled rice acquire multiple neuritis in some cases.
11. Fowls kept entirely without food and those which are given all they will eat of polished rice lose weight with almost equal rapidity in the great majority of cases.
12. A loss of at least 21 per cent of the body weight almost invariably occurs before any signs of multiple neuritis become apparent.
13. The signs, symptoms, and nerve appearances are identical in neuritis produced by inanition and in that caused by feeding polished rice.
14. Spasticity is a late symptom in some fowls which develop neuritis and are then saved from death by the institution of mixed feeding.
15. In neuritis-producing rice and in beriberi-producing dietaries both the phosphorus and the potassium are markedly reduced in amount, the latter in greater degree than the former.
16. As an *index* of the beriberi-producing power of a given rice, reduction in the potassium content is probably quite as reliable as reduction in the phosphorus content.



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TABLE IV.—*Individual numbers of fowls and percentages of weight gained or lost during experiments.*

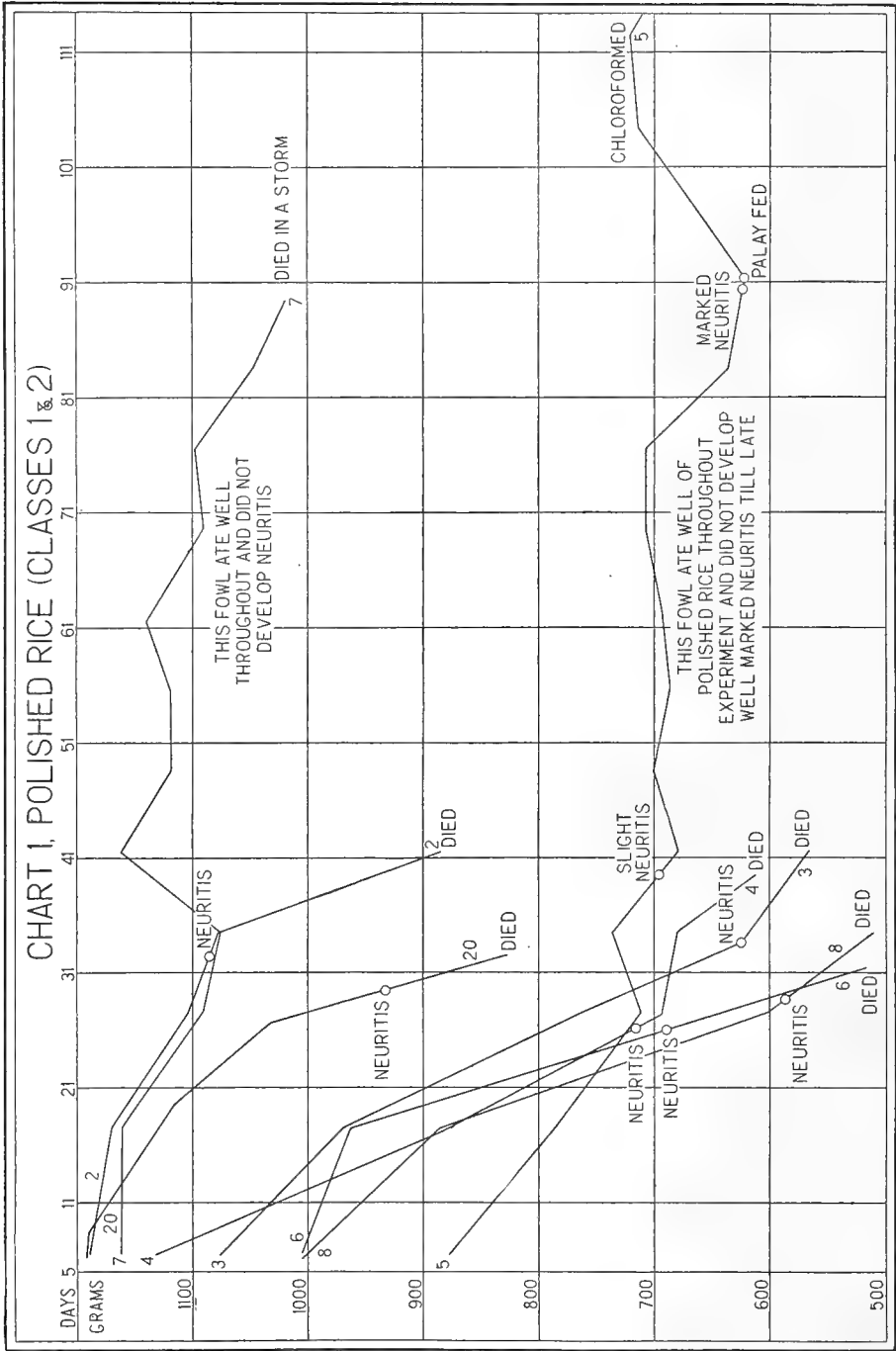
Food			Individual number of fowl.	Weight at beginning.	Weight at appearance of signs of neuritis.	Percentages lost to appearance of signs.	Weight at end.	Percentage lost to end.	Percentage gained to end.	Developed polyneuritis.	Remained well.	Died of other disease.
Group A: Polished rice.	Alone.	Class 1: Filipino No. 1.	<sup>a</sup> 1	Gms. (b)	Gms.		Gms. (b)					1
			2	1,190	1,077	9.5	885	25.7		1		
			3	1,077	623	42.2	566	47.5		1		
			4	1,133	700	38.3	623	45.1		1		
			20	1,218	1,034	15.2	828	32.1		1		
		Class 2: Saigon, Subsistence Department.	5	878	680	22.6	623	29.1		1		
			6	1,006	650	35.4	517	48.7		1		
			<sup>c</sup> 7	1,162			1,020	12.3				1
			8	1,006	602	40.2	510	49.4		1		
		Class 3: Saigon 118 grams daily by force when necessary.	40	956			1,006		5.2		1	
			45	921	574	37.7	568	38.4		1		
			48	1,204	751	37.7	736	38.9		1		
			49	1,119	700	37.5	623	44.4		1		
	With various salts.	Class 4: 0.05 gram KCl daily.	21	1,112	865	22.3	722	35.1		1		
			22	1,218	914	25.0	744	39.0		1		
			23	1,268	864	31.9	637	49.8		1		
			24	970	650	33.0	474	51.2		1		
		Class 5: 0.03 gram H <sub>3</sub> PO <sub>4</sub> daily.	25	1,013	779	23.2	700	30.9		1		
			26	1,140	800	29.9	708	37.9		1		
			28	1,021	700	31.5	489	52.2		1		
		Class 6: 0.06 gram H <sub>3</sub> PO <sub>4</sub> daily.	59	1,226	970	20.9	871	29.0		1		
			60	1,176	830	29.5	807	31.4		1		
			<sup>a</sup> 61	1,261			828	34.4				1
		Class 7: 0.05 gram KCl and 0.03 gram H <sub>3</sub> PO <sub>4</sub> daily.	29	1,091	857	21.5	687	37.1		1		
			<sup>a</sup> 30	1,091			(b)					1
			31	1,091	779	28.6	700	35.9		1		
			32	1,070	566	47.2	538	49.8		1		
			<sup>a</sup> 37	991			651	34.4				1
		Class 8: 0.03 gram H <sub>3</sub> PO <sub>4</sub> followed by 0.05 gram KCl daily.	27	1,098			998	9.2			1	

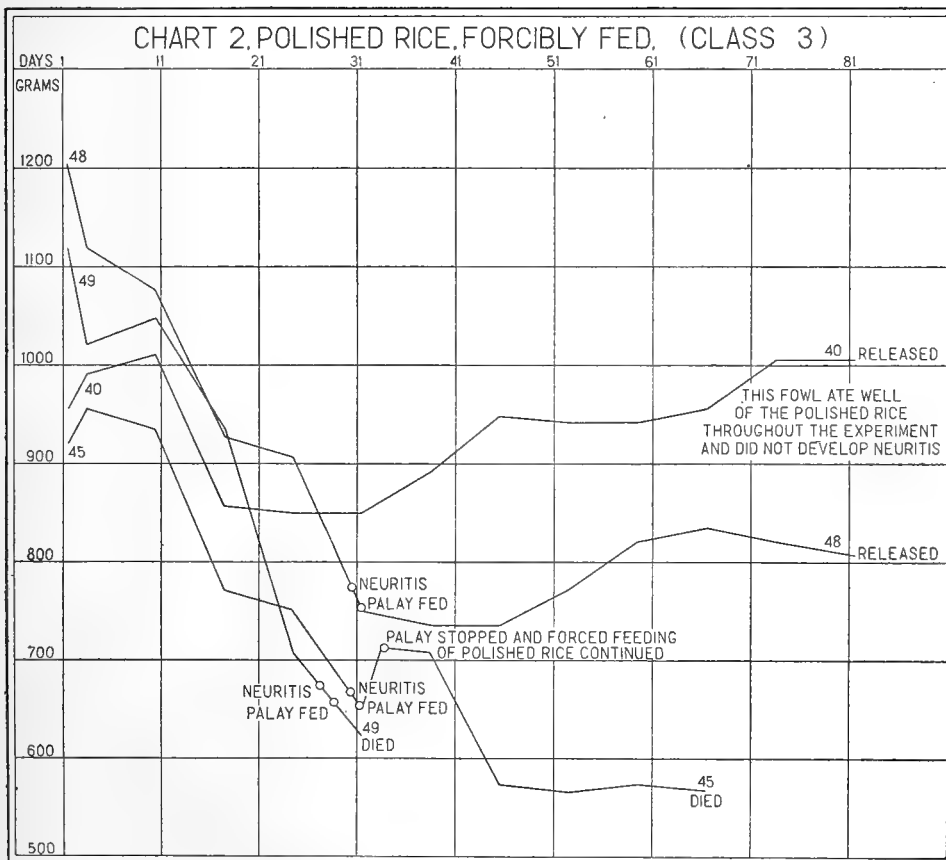
<sup>a</sup> Died of avian diphtheria.<sup>b</sup> Not known.<sup>c</sup> Found dead after a storm.

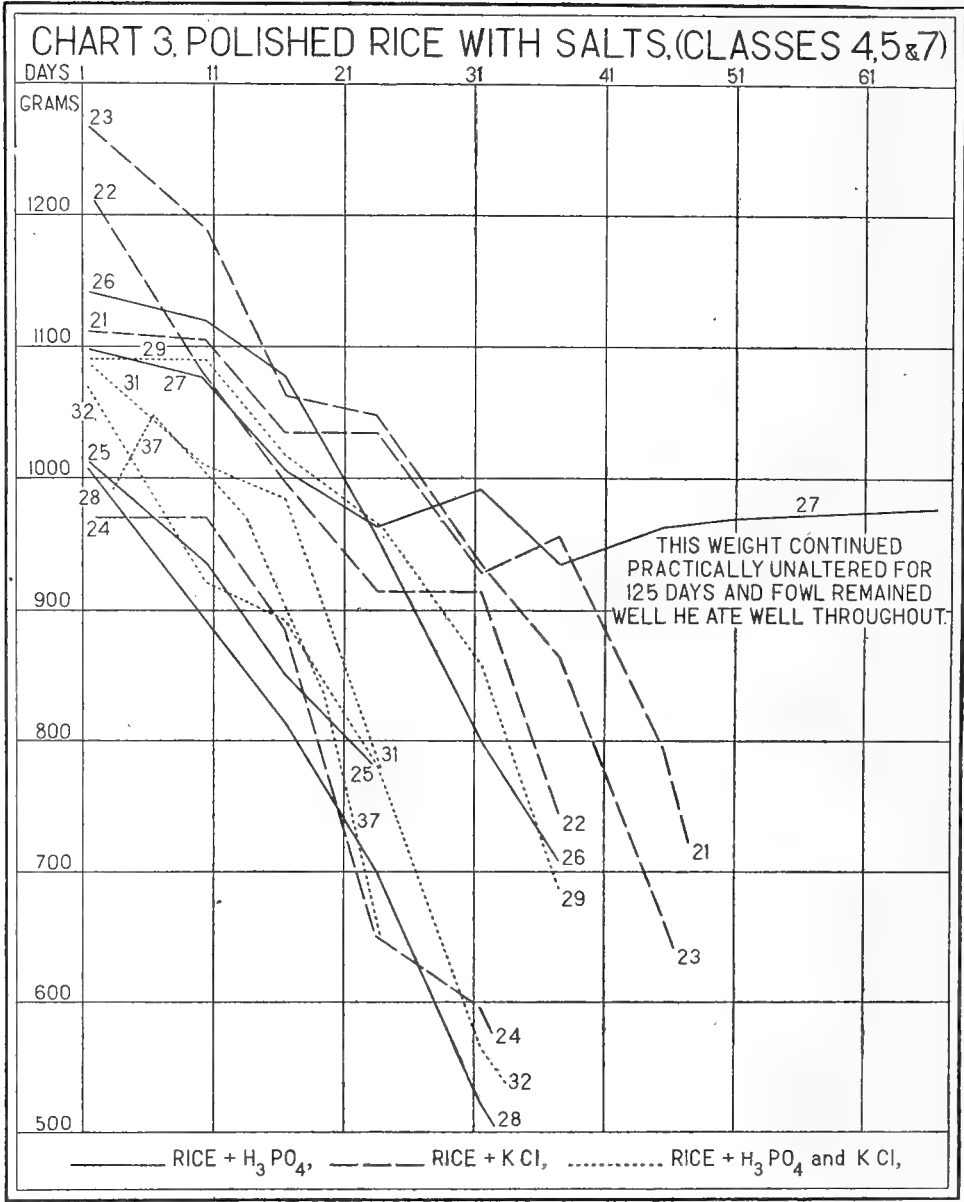
TABLE IV.—*Individual numbers of fowls and percentages of weight gained or lost during experiments—Continued.*

Food.			Individual number of fowl.	Weight at beginning.	Weight at appearance of signs of neuritis.	Percentage lost to appearance of signs.	Weight at end.	Percentage lost to end.	Percentage gained to end.	Developed polyneuritis.	Remained well.	Died of other disease.
Group B: Under-milled rice.	Alone.	Class 9: Filipino with yellow pericarp.	9	Gms. 907	Gms. —	—	Gms. 751	17.2	—	—	1	—
			10	1,048	—	—	1,112	—	6.1	—	1	—
			11	1,105	—	—	1,303	—	17.9	—	1	—
			12	978	—	—	1,020	—	4.2	—	1	—
		Class 10: Filipino with red pericarp, Subsistence Department.	38	1,176	—	—	1,445	—	22.8	—	1	—
			39	921	—	—	1,176	—	27.6	—	1	—
			<sup>a</sup> 46	1,119	—	—	659	41.1	—	—	—	1
			47	1,042	—	—	1,431	—	37.3	—	1	—
	With salt.	Class 11: Filipino (yellow) + 0.36 gram NaCl daily.	33	1,028	—	—	850	17.4	—	—	1	—
			<sup>a</sup> 34	1,155	—	—	850	26.5	—	—	—	1
			35	1,261	—	—	1,374	—	9.0	—	1	—
			36	1,091	—	—	1,282	—	17.5	—	1	—
			<sup>d</sup> 58	871	—	—	715	18.0	—	—	<sup>e</sup> 1	—
			—	—	—	—	—	—	—	—	—	—
Group C: Unhusked rice.	Alone.	Class 12: Filipino Macan rice ( <i>palay</i> ).	13	1,133	—	—	1,197	—	5.6	—	1	—
			14	1,077	—	—	885	17.9	—	—	1	—
			15	1,119	—	—	1,126	—	.6	—	1	—
			16	907	—	—	736	18.9	—	—	1	—
Group D: Starvation.	Reduced under-milled.	Class 13: $\frac{1}{2}$ allowance.	18	1,006	538	46.6	510	49.4	—	1	—	—
		Class 14: $\frac{1}{4}$ allowance.	19	842	550	34.7	510	39.5	—	1	—	—
	Absolute.	Class 15: Water only.	17	991	722	27.2	595	40.0	—	1	—	—
			<sup>a</sup> 41	793	—	—	481	39.4	—	—	—	1
			<sup>f</sup> 42	963	—	—	524	45.6	—	—	—	1
			<sup>g</sup> 43	907	—	—	566	37.6	—	—	—	1
			44	970	582	40.0	531	45.3	—	1	—	—
			<sup>b</sup> 54	907	—	—	637	29.8	—	—	—	1
			55	963	700	27.4	700	27.4	—	1	—	—
			<sup>h</sup> 56	991	—	—	550	44.6	—	—	—	1

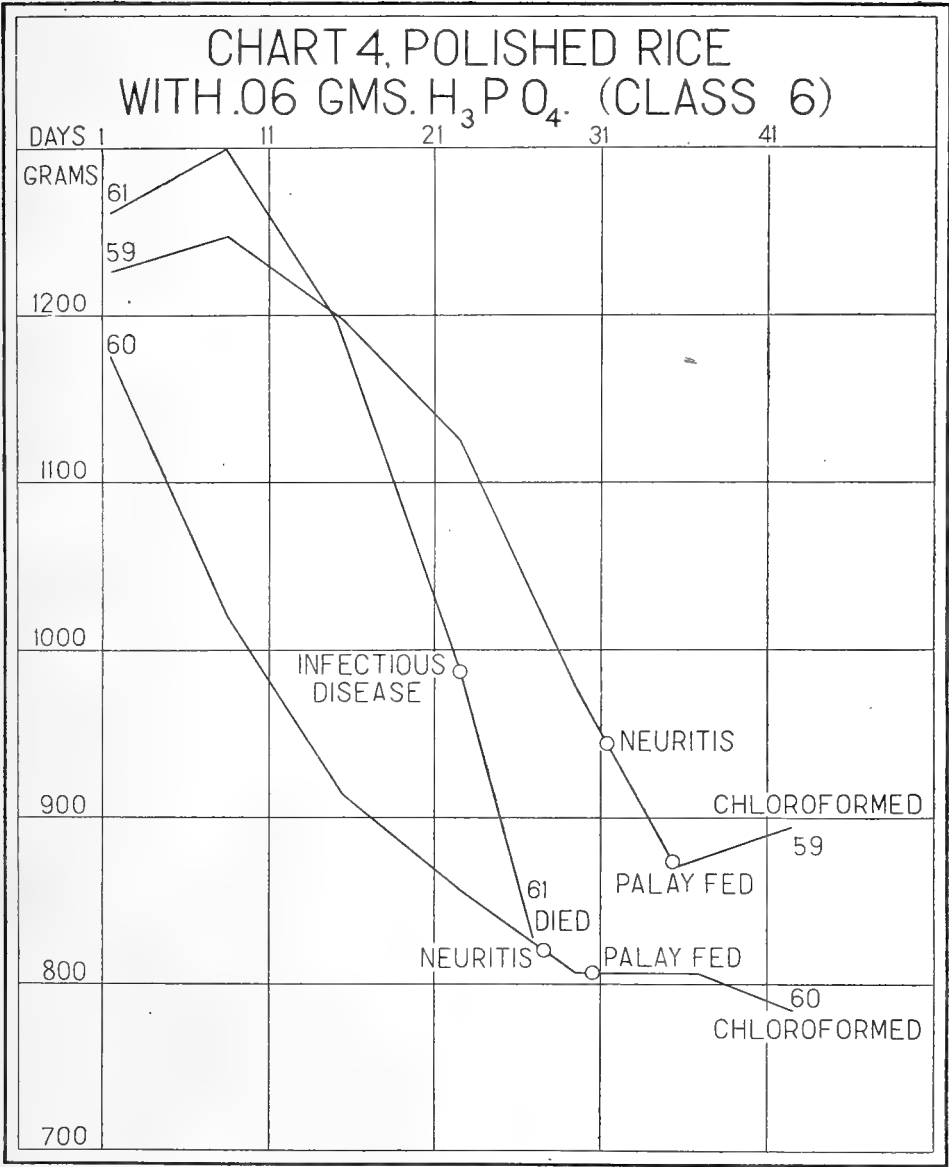
<sup>a</sup> Died of avian diphtheria.<sup>b</sup> Not known.<sup>c</sup> Found dead after a storm.<sup>d</sup> Sick with avian diphtheria.<sup>e</sup> Recovered.<sup>f</sup> Died of starvation carried too far.<sup>g</sup> Cause of death unknown.<sup>h</sup> Died of starvation.

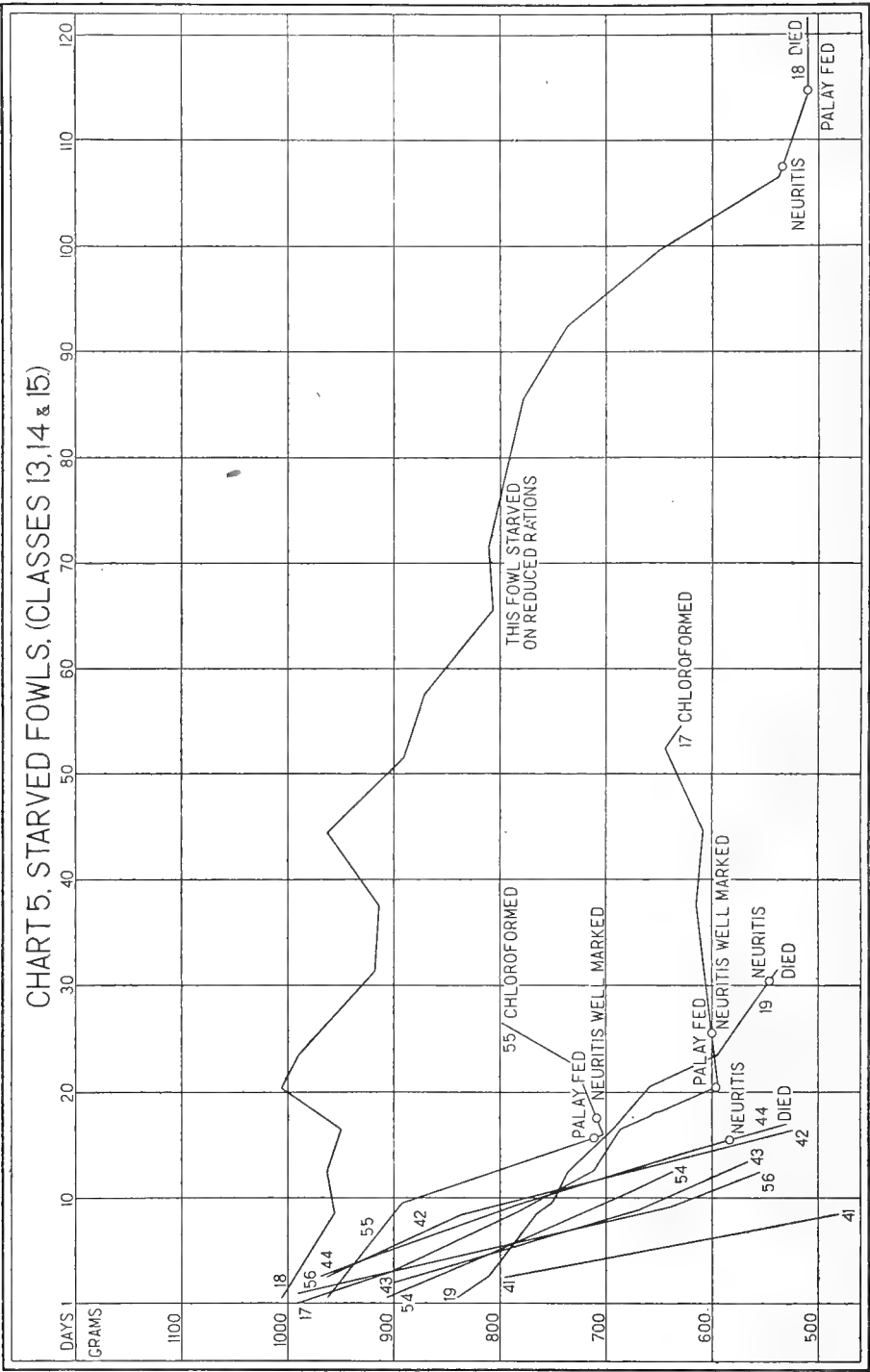












## ILLUSTRATIONS.

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### PLATE I.

- FIG. 1. Cages used for fowls during experiments.  
2. Fowl number 5 in spastic stage. Shows extreme extension at knees and a tendency to teeter forward.  
3. Fowl number 5 in spastic stage. Shows extreme extension at knees and a tendency to teeter forward.

### PLATE II.

- FIG. 4. Front view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.  
5. Profile view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.  
6. Fowl number 6. Late stage of neuritis resulting from a diet of polished rice.  
7. Front view of fowl number 8 showing neuritis resulting from polished rice diet.

### PLATE III.

- FIG. 8. Profile view of fowl number 8 showing neuritis resulting from polished rice diet.  
9. Front view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop.  
10. Profile view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop and leg signs.  
11. Front view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 4.

### PLATE IV.

- FIG. 12. Profile view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 5.  
13. Front view of fowl number 55 showing early appearances in neuritis produced by starvation. Compare with Plate II, figure 4.  
14. Profile view of fowl number 55 showing earliest appearances in neuritis produced by starvation.





FIG. 1.—Cages used for fowls during experiments.

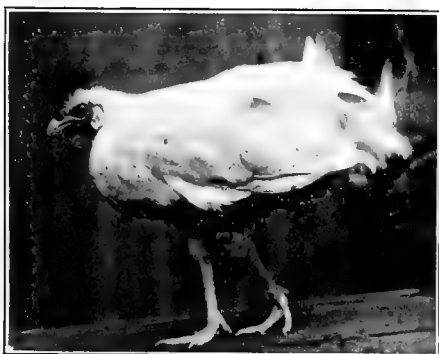


FIG. 2.—Fowl number 5 in spastic stage.  
Shows extreme extension at knees and  
a tendency to teeter forward.



FIG. 3.—Fowl number 5 in spastic stage.  
Shows extreme extension at knees and  
a tendency to teeter forward.

PLATE I.





FIG. 5.—Profile view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.



FIG. 6.—Fowl number 6. Late stage of neuritis resulting from a diet of polished rice.



FIG. 7.—Front view of fowl number 8 showing neuritis resulting from polished rice diet.



FIG. 4.—Front view of fowl number 6 showing well-developed neuritis resulting from a diet of polished rice.







FIG. 8.—Profile view of fowl number 8 showing neuritis resulting from polished rice diet.



FIG. 9.—Front view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop.



FIG. 10.—Profile view of fowl number 18 which developed neuritis from starving on reduced rations. Shows wing-drop and leg signs.



FIG. 11.—Front view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 4.





FIG. 12.—Profile view of fowl number 17 showing late appearances in neuritis produced by starvation. Compare with Plate II, figure 5.



FIG. 13.—Front view of fowl number 55 showing early appearances in neuritis produced by starvation. Compare with Plate II, figure 4.



FIG. 14.—Profile view of fowl number 55 showing earliest appearances in neuritis produced by starvation.

PLATE IV.



## A STUDY OF THE INTESTINAL PARASITES FOUND IN CAVITE PROVINCE.<sup>1</sup>

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By E. R. STITT.<sup>2</sup>

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An out-patient department where medical aid has been given such Filipino patients as might present themselves, has been in operation during the year 1910 at the United States naval hospital, Cañacao, Cavite Province.

The 932 stool examinations upon which the statistics to follow are based, were therefore made upon specimens from cases of sick people and of these only such patients as it was thought required such an examination for diagnostic reasons were made to bring such a specimen of faeces.

The patients presenting themselves at our clinic come almost exclusively from the city of Cavite and the adjacent towns of Caridad and San Roque. The conditions as regards rainfall and soil considerations are therefore the same for all of them. The rainfall in Cavite is slightly less than in Manila, where the yearly average approximates 75 inches. In this connection it should be stated that practically 80 per cent of the rain of the year falls in the months from June to October. Even after the most severe tropical rainfall the ground becomes dry in a very few hours. The average yearly temperature is about 27° C. and the difference between the average temperature of the coldest and hottest months is only about 4° C.

The towns of Cavite, San Roque, and Caridad are situated on a low-lying sandy peninsula, the soil being chiefly coarse-grained sand. Many of the lower levels are covered at high tide with salt water from the adjacent waters of Cañacao and Manila Bay.

These statements as to soil and climatic conditions are presented in view of a probable explanation of the small number of hookworm infections noted in our stool examinations.

Of the 932 examinations, 135 or 14.4 per cent failed to show the

<sup>1</sup>Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, February 24, 1911.

<sup>2</sup>Surgeon, United States Navy, associate professor of medical zoölogy, Department of Tropical Medicine, College of Medicine and Surgery, University of the Philippines, Manila, P. I.

presence of intestinal parasites or their ova. The remaining positive examinations gave findings as follows:

Organism.	Number of in- fections.	Per cent.
<i>Ascaris</i> .....	627	67.2
<i>Trichocephalus</i> .....	607	65.1
Flagellates .....	135	14.4
Amœbæ .....	111	10.9
Hookworm .....	23	2.4
<i>Tænia saginata</i> .....	3	.3
<i>Balantidium</i> .....	1	.1
<i>Strongyloides</i> .....	1	.1

I personally, and very carefully, made the stool examinations in 100 of the above cases taken in sequence, using neutral red as well as with ordinary cover glass preparations, and obtained the following results:

Age.	Cases.	<i>As- caris.</i>	Whip- worm.	Hook- worm.	<i>Amœ- bæ.</i>	Flagel- lates.
Under 5 years .....	42	37	28	0	2	2
5 to 10 years .....	27	25	23	0	2	5
10 to 25 years .....	16	9	14	1	2	1
25 to 50 years .....	10	8	4	0	2	1
Over 50 years .....	5	1	3	0	1	1
Total .....	100	80	72	1	9	10

Twelve of the cases tabulated above failed to show intestinal parasites or their ova. Of the entire total, positive for hookworm, 8 were between 5 and 15 years of age; 7 were between 25 and 35; 4 between 15 and 25; 3 over 35, and only 1 under 5 years.

Among the specimens positive for amœbæ there were organisms which as regards ectosarc characteristics and distribution of nuclear chromatin corresponded to *Entamœba coli* and *Entamœba histolytica*. Both types would frequently be observed in the same stool. Very few of these amœbic infections presented dysenteric or other symptoms. However, in three cases with marked anæmia and loss of energy and with the presence of very great numbers of amœbæ in the stools, ipecac treatment caused the disappearance of amœbæ and complete restoration to health.

We find, on comparing the percentage of cases positive for amœbæ with the results of examinations of the members of the Hospital Corps of the United States Navy on duty at this hospital, that an examination of the stools of 26 of these native-born Americans, in August, 1910, showed 34 per cent to be infected. A similar examination of 33 cases in December, 1910, gave positive findings for amœbæ in 37 per cent. There are certain points to be kept in mind in judging of the greater

frequency of amœbiasis in these members of the Naval Hospital Corps as compared with that in the Filipino patients examined.<sup>3</sup>

*First:* The stools of the men in the hospital corps were examined within a short time after being passed. It is a matter of common observation that a stool showing many amœbæ may, after standing for a few hours, fail to show the presence of a single amœba. Many of the specimens brought to the laboratory by Filipino patients were evidently many hours old.

*Second:* The expedient of giving a dose of salts prior to examination for amœbæ was not practicable with the Filipinos.

*Third:* Our experience has been that amœbæ are less frequent in young children and as about one-third of our Filipino patients were of such age, this should be taken into consideration.

At Bilibid Prison, Garrison encountered amœbic infection in 23 per cent of the cases.<sup>4</sup> In the medical survey of Taytay, his findings were 2.7 per cent.<sup>5</sup> Rissler and Gomez<sup>6</sup> report only 0.39 per cent of amœbic infection in their examinations in Las Piñas and no cases showing such infections in Tuguegarao and Santa Isabel. Such numbers are in striking contrast with those of former investigators, some of whom have reported as high a percentage of infection as 70.

Our findings as regards flagellates (14.4 per cent) correspond fairly closely with those of Garrison, namely, 21 per cent at Bilibid and 5.5 per cent at Taytay.

Repeated examinations with Giemsa staining and the counting of flagella in preparations in wet Gram solution showed only one species of flagellate to be present, *Trichomonas intestinalis*. *Lambliæ* was not found in a single instance.

Garrison, for *Trichocephalus* infection, obtained 59 per cent at Bilibid and 77 per cent at Taytay; Rissler and Gomez give 53 per cent at Las Piñas; 25.9 per cent at Tuguegarao, and 6.23 at Santa Isabel. Our findings were 65.1 per cent.

As regards *Ascaris* we found a higher rate of infection than for any other parasite (67.2 per cent). Garrison encountered 26 per cent at Bilibid and 82.9 per cent at Taytay. The percentages of Rissler and Gomez are 77, 73, and 60 respectively for Las Piñas, Tuguegarao, and Santa Isabel.

Garrison noted at Bilibid an incidence second only to *Trichocephalus* for hookworm infection, namely 52 per cent. His percentage of infection at Taytay was 11.6. Rissler and Gomez found 11.14 of all cases examined, infected with hookworms at Las Piñas; 8.01 per cent in Tuguegarao, and 45.38 per cent in Santa Isabel. We noted only 2.4 per cent for Cavite, San Roque, and Caridad.

<sup>3</sup>Thirty-five and six-tenths per cent as against 10.9 per cent for Filipinos.

<sup>4</sup>*This Journal*, Sec. B (1908), 3, 191.

<sup>5</sup>*Ibid.* (1909), 4, 257.

<sup>6</sup>*Ibid.* (1910), 5, 267.

The soil conditions mentioned above probably to a great extent account for the low incidence of hookworm disease as brought out in our examinations. Instead of a fine-grained, sandy soil which holds moisture tenaciously<sup>7</sup> we have here a coarse-grained sand which dries up completely almost as soon as the rain stops falling. Stiles attaches importance to the consideration that a wooded location is favorable to the development of hookworms because the shade of the trees counteracts the injurious effects of drying on the larvæ. There are practically no shade trees in this section. The frequent flooding of low-lying sections with sea water at the time of high tides must also influence the possibility of infection.

Our findings as regards *Strongyloides* (0.1 per cent) were far below those reported by Garrison at Bilibid (3 per cent) and at Taytay (0.7 per cent). Rissler and Gomez found 2.24 per cent infected in Las Piñas, but no cases were encountered in Tuguegarao and Santa Isabel. The same factors influencing hookworm infection in this locality may be operative for *Strongyloides*. Garrison found 0.2 per cent of the individuals examined at Taytay to be infected with ciliates, while Gomez and Rissler failed to find such infections at Tuguegarao or Santa Isabel. We found a single case in the 932 examinations.

Our three cases of tapeworm infection were with *Tænia saginata*.

<sup>7</sup> Views of Nicholson and Rankin as to favorable soil for hookworm development.



# THE DYSENTERY BACILLUS WITH A BACTERIOLOGIC STUDY OF AN EPIDEMIC OF BACILLARY DYSENTERY IN THE PHILIPPINES.

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By EUGENE R. WHITMORE.<sup>1</sup>

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

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Shiga,<sup>(1)</sup> in 1908, announced that he had cultivated a special bacillus from the stools of dysentery patients and considered this bacillus to be the specific cause of bacillary dysentery. Since that time much attention has been given to the study of bacteria in the stools of patients suffering from dysentery.

In 1900, Flexner<sup>(2)</sup> and Strong<sup>(3)</sup> described a similar or identical bacillus in the stools of dysentery patients in Manila and almost at the same time Kruse<sup>(4)</sup> gave an account of a similar one in the same class of material in Germany. He rightly described the bacillus as non-flagellated, while Shiga called it a motile bacillus with flagella. From this time on the number of observations on the bacteria found in the stools of patients suffering with diarrhœa and dysentery increased very rapidly, and very soon workers began to note that there were differences between the bacteria isolated in various places, and between the bacteria isolated from different cases in the same place. Kruse considered his bacillus to be different from the Shiga-Flexner organism<sup>2</sup> because it was non-motile and without flagella.

Koch suggested that a commission should compare the various strains of the dysentery bacillus isolated by different men. This was done, and the Shiga, Flexner, Kruse, and two Döberitz strains were found to be morphologically and culturally alike. None of them bore flagella, while all of them showed a marked oscillating molecular motion. However, the Flexner strain did not agglutinate as strongly with the serum of a convalescent patient in the Döberitz epidemic as did the others.

Several observers, following this work, described dysentery-like bacilli which were found in various dysenteric conditions, especially in asylum dysentery. These organisms resembled the true bacilli of dysentery in cultures and in hanging drops, and they were agglutinated in as high dilutions of the serum of convalescent dysentery patients as were the true dysentery strains. However, staining showed them to have flagella, and further growth on different culture media proved them to be different from the true dysentery bacilli. From this it was evident that the serum of convalescent dysentery patients could not be used for the differentiation of dysentery and dysentery-like bacilli.

Martini and Lentz<sup>(5)</sup> immunized animals to two different strains of the

<sup>1</sup>Major, Medical Corps, United States Army; detailed to the Biological Laboratory, Bureau of Science, Manila, P. I.

<sup>2</sup>Flexner described his organism as a motile bacillus with flagella, while Strong was not able to demonstrate flagella.

dysentery bacillus and tested the agglutinating power of the different specific sera on the various strains. They also made a careful study of the morphology and cultural properties of the latter. They began by attempting to immunize rabbits and guinea pigs to seven strains, but so many animals died that they abandoned this method. Rabbits resisted one strain of the Flexner organism, and a good serum was obtained. Martini and Lentz then immunized a goat to the strain "Shiga," and prepared a very active serum.

They were able to show from the agglutination reactions with these sera that the Shiga, Kruse, and eight other strains were identical (Group I), while the Flexner and Strong strains from the Philippines differed from the latter (Group II). It was further proved that one of Strong's strains differed from the Flexner in its agglutinability, although Martini and Lentz do not seem to have made it into a separate group at that time, but left it with the Flexner, pseudodysentery (Kruse), and several others, all of which were different from the Shiga and Kruse types.

Hiss and Russell(6) described a bacillus which they isolated from a fatal case of diarrhœa in a child. They called this organism "Bacillus dysenterix Y" and it soon was shown that the bacillus of asylum dysentery was identical with this variety.

It does not appear that Martini and Lentz tested the agglutinability of bacillus Y to their "Flexner" serum, although they seem to have had it in their series (Pseudodysentery Kruse) and found that it did not agglutinate with their Shiga serum. Since we know now that the serum from the Flexner organism often agglutinates Bacillus Y in as high dilution as it does the Flexner, it would have been interesting to have studied this question.

Hiss and Russell differentiated their Bacillus Y from the Shiga bacillus by means of mannite- and maltose-litmus agar, and almost at the same time Lentz(7) used these same media for the differentiation of dysentery and dysentery-like bacilli. He worked with the strains which Martini and Lentz had used in their agglutination experiments. By means of the sugar media, he was able to show that one of Strong's strains was different from that of Shiga and Flexner, while the two latter were also proved to be different from each other by their behavior in the sugar media. This corresponded to the finding of Martini and Lentz, as a result of their studies of the agglutination reactions of the same three strains.

This brief review of the literature shows that the dysentery bacillus had been divided into four groups by the use of sugar media and that three of these groups were also distinct in their agglutinability.

The following table gives the cultural differences in sugar media that are relied upon for isolation of the dysentery bacillus and to separate it into types:

*Cultural differences in sugar media.*

Litmus agar with addition of—	Appearance in culture of bacillus.			
	Shiga-Kruse.	Y.	Flexner.	Strong.
Lactose.....	Blue.	Blue.	Blue.	Blue.
Dextrose.....	Red.	Red.	Red.	Red.
Mannite.....	Blue.	Red.	Red.	Red.
Maltose.....	Blue.	Blue.	Red.	Blue.
Saccharose.....	Blue.	Blue.	Blue.	Red.

Three of these types (Shiga, Flexner, and Strong) correspond exactly to the agglutination reactions, while the other one (Bacillus Y) is only irregularly differentiated from that of Flexner by that reaction. Furthermore, the action on mannite corresponds to a difference in toxicity; the Shiga-Kruse type which does not *produce acid in mannite*, is very toxic for animals, while the other types which *produce acid in mannite* are not nearly as toxic. This difference in toxicity was clearly shown by Martini and Lentz at the time they differentiated their two groups on the basis of the agglutination reactions.

A number of other types have been added at times, and the above have been separated into a number of others by various workers. Thus Shiga(8) made a fifth type which differed from the "Flexner" in that it produced acid in mannite in the first twenty-four hours, and then alkali. It was very close or similar to the Flexner type in all other properties, including agglutinability. Ohno(9) grew a large number of strains of the dysentery bacillus in the sugars for fourteen days and in this way divided the dysentery bacillus into 15 varieties because of their action on the sugars; but when he tested the agglutinability of his various strains he did not observe these varieties.

Hetsch(10) already had pointed out that the reaction differed somewhat according to the percentage of sugar in the medium. In addition to sugar, the media contain peptone and albumoses, and while the decomposition products of the sugars are mainly acid, those of the peptone and albumoses are mainly alkaline. The bacteria attack both classes of substances and upon the amount of one or the other present, as well as the avidity with which one or the other is attacked, depends the acidity or alkalinity of the sum total of the products of decomposition. Again, an organism may change in its relative avidity for the carbohydrate and the proteid content of the medium. Hiss and Russell(6) and a number of others have shown that an organism may change in its action on sugars after it has been on artificial media for some time.

Finally, the absorption experiment of Castellani has been used for the separation of the dysentery bacillus into types, but it gives so many that it almost hopelessly complicates the placing of any particular strain.

During an epidemic of bacillary dysentery in the Philippines occurring in the summer of 1909, I was able to isolate dysentery and dysentery-like bacilli from the stools of a number of cases, and I proceeded to study the organisms along the lines indicated in the foregoing review of the literature. In isolating the organisms, I tried the various lactose-agar media, but did not find any of them to be superior to the litmus-lactose-agar for practical work on the dysentery bacillus.

I prepared my plates in the laboratory in Manila, took them with me into the provinces where the dysentery was most active, streaked the plates there and then brought them back to the laboratory with me, or else, when I remained in the provinces for a few days, I picked colonies and transplanted them into tubes before coming back. In this way I was able to isolate a bacillus of the Shiga-Kruse type from 12 out of 40 cases of severe, acute dysentery in natives of two towns of Batangas Province where there was an epidemic of acute dysentery with a high

mortality.<sup>3</sup> No other strain of the dysentery bacillus was found by me in that locality. I was able four times to isolate a bacillus of the Flexner-Strong type and one of the Shiga-Kruse type once from sporadic cases of acute dysentery around Manila. Besides this, I obtained a large number of dysentery-like bacilli.

These organisms were determined by the cultural characteristics, including their reactions in sugar media, their pathogenicity for lower animals, and their agglutination reactions with sera of animals immunized to known strains of the various types of the dysentery bacillus. As all but one of the strains of the Shiga-Kruse type came from one locality and all of them were identical, I chose the Manila strain (P. S. II) and one of the Batangas strains (P. S. I). In the same way I selected two of the Flexner-Strong strains (P. A. I. and P. A. II) and six of the dysentery-like organisms (L. I. to L. VI). As my further work in agglutination reactions was to immunize animals to each strain and then to test the agglutinability of every strain with every serum, it was manifestly necessary for me to keep the number within working limits, and there was no necessity of working with a large series that culturally and by agglutination reactions had been shown to be identical. Again, reasonable economy in animals required that I should not use too many strains, especially as I was working with rabbits, and my Shiga-Kruse strains were so virulent for them that I lost a number of animals before I prepared a serum that agglutinated in sufficiently high dilution to be of any value.<sup>4</sup>

The following chart gives the morphology and cultural character of the strains chosen by me for further work, as well as two of the Shiga-Kruse type (S. S. I and S. S. II) and one of the Flexner (S. A. II), kindly sent to me by Professor Shiga, and one strain of the Flexner-Strong type (S. A. I) brought from Heidelberg by Doctor Coca.

I also tried Jehle and Charleton's<sup>(11)</sup> serum medium with the sugars. The result was entirely in accord with the findings on agar.

From the following chart it can be seen that the first four strains fall in the Shiga-Kruse type, while the next four belong to that of Flexner-Strong. The last six easily are shown not to be dysentery bacilli at all. There is no example of the Bacillus Y.

<sup>3</sup> I took blood from each patient for agglutination tests, at the time that I obtained the stool. The blood-sera of patients who had been sick less than three days did not agglutinate the dysentery organisms; the sera from those who had been ill three to five days agglutinated slightly, or not at all, while that from patients who had been ill over five days agglutinated from 1:40 to 1:100, but no special work was done in this line, as the patients' sera were not depended upon at all for determining the organisms.

<sup>4</sup> Martini and Lentz say that the serum should agglutinate in a 1:300 dilution.

CHART A.

Culture.	Size and form.	Motility.	Flagella.	Indol production.	Properties of growth on—							
					Plain agar.	Litmus-lactose agar.	Litmus-dextrose agar.	Litmus-mannite agar.	Litmus-maltose agar.	Litmus-archarose agar.	Litmus milk.	Bouillon.
P. S. I.	Short plump bacillus.				White, spreading slightly.	No change.	Acid.	Alkaline.	Alkaline.	Alkaline.	Slightly acid, not coagulated.	Cloudy, with tendency to settle. No scum on top.
P. S. II.	do.				do.	do.	do.	do.	do.	do.	do.	Do.
S. S. I.	do.				do.	do.	do.	do.	do.	do.	do.	Do.
S. I. II.	do.				do.	do.	do.	do.	do.	do.	do.	Do.
P. A. I.	do.			Trace.	do.	do.	do.	Acid.	Acid.	do.	do.	Do.
P. A. II.	do.				do.	do.	do.	do.	do.	do.	do.	Do.
S. A. I.	do.			Trace.	do.	do.	do.	do.	do.	do.	do.	Do.
A. A. II.	do.				do.	do.	do.	do.	do.	do.	do.	Do.
L. I.	do.				Yellowish after 3 days.	do.	Acid, decoloration at bottom.	Alkaline.	Alkaline.	do.	Alkaline, not coagulated.	Heavy sediment.
L. II.	do.				Like P. A. I.	do.	Acid.	Acid slight.	Acid.	No change.	do.	Like P. A. I.
L. III.	Longer than above.				Richer growth.	do.	do.	Alkaline.	Alkaline.	Alkaline.	do.	Rich growth, heavy sediment.
L. IV.	Short plump bacillus.				Like P. A. I.	do.	Acid slight.	do.	Acid.	do.	do.	Like P. A. I.
L. V.	Longer than above.			Slight.	Rich growth white.	do.	Acid, decoloration at bottom.	No change.	Decolorized.	No change.	Decolorized, not coagulated.	Heavy sediment, scum on top.
L. VI.	do.			Slight.	do.	do.	do.	do.	do.	do.	do.	Do.

<sup>a</sup> Became slightly acid after six weeks.

Using the four Shiga-Kruse strains, I attempted to determine their type according to Ohno's method. Two of my strains (P. S. I and P. S. II) were isolated recently, while two (S. S. I and S. S. II) had been on artificial media for some time. All of the four belonged in Ohno's type A. Eight months later I tested these same strains again. One (P. S. II) had changed to Ohno's type B, while the other three remained in his type A.

I used rabbits for the preparation of specific sera and made all injections intravenously. The animals were weighed once a week and the injections were given as closely as possible within the same interval, consideration being given to the weight and general conditions of the animal.

The first four or five injections were of organisms grown in agar for 18 hours and heated to 60° for one hour, while the later ones were of living organisms. Each animal usually received fourteen injections. The first was always very small and later the dose gradually was increased. I had great difficulty with the rabbits which were given the Shiga-Kruse cultures, 1/50 of a loop of a killed culture of one of the recently isolated strains killing rabbits when injected intravenously. I lost animals from the use of these strains as late as the fourteenth injection. The two strains received from Japan were not so virulent, possibly because they had been on artificial media for some time. The animals withstood larger doses of the latter and this may account for the fact that I attained sera with stronger agglutination from them. These facts appear in the agglutination tables given below. No especial difficulty was encountered in giving the Flexner strains and non-dysentery organisms in much larger doses than is possible with the Shiga-Kruse strains.<sup>5</sup>

The animals were bled about ten days after the last injection. In order to obtain the large amount of serum needed for this work and still not to kill the rabbit, the following method was used:

A large test tube was provided with a rubber stopper having two perforations. A piece of glass tubing connected by a short piece of rubber tubing to a long, slender aspirating needle passed through one perforation; a piece of glass tubing through the other, the latter connected with the vacuum apparatus by a long piece of rubber tubing. The rabbit was placed on its back on an animal board,

<sup>5</sup> At the same time I immunized a horse to both Shiga-Kruse and Flexner types, by giving weekly intravenous injections of living organisms alternating with the filtrate from an old culture in alkali bouillon. One horse died of an intercurrent condition after it had received ten injections, but another received seventeen injections and at the end of that time his blood agglutinated Shiga at 1:800 and Flexner above 1:1000. The animal was bled ten days after the last injection and the serum put up for use in the treatment of bacillary dysentery. So far we have had very little opportunity to try it, as the epidemic dysentery under discussion was over by the time the serum was ready for use.







TABLE IV.

[illegible]

TABLE V.

[illegible]



TABLE VIII.

[illegible]

TABLE IX.

[illegible]

TABLE X.

Culture.	Is agglutinated in rabbit serum L. I in a dilution of —										
	1:10.	1:20.	1:50.	1:100.	1:200.	1:300.	1:400.	1:500.	1:600.	1:700.	1:800.
P. S. I	—	—	—	—	—	—	—	—	—	—	—
P. S. II	—	—	—	—	—	—	—	—	—	—	—
S. S. I	—	—	—	—	—	—	—	—	—	—	—
S. S. II	—	—	—	—	—	—	—	—	—	—	—
P. A. I	+	—	—	—	—	—	—	—	—	—	—
P. A. II	±	—	—	—	—	—	—	—	—	—	—
S. A. I	±	—	—	—	—	—	—	—	—	—	—
S. A. II	±	±	—	—	—	—	—	—	—	—	—
L. I	+	+	+	+	+	+	+	+	+	+	±
L. II	±	—	—	—	—	—	—	—	—	—	—
L. III	—	—	—	—	—	—	—	—	—	—	—
L. IV	+	—	—	—	—	—	—	—	—	—	—
L. V	+	—	—	—	—	—	—	—	—	—	—
L. VI	+	—	—	—	—	—	—	—	—	—	—

From the foregoing tables it is evident that the first four strains are identical; also that the next four are identical among themselves, but are entirely different from the first four. Two of the first four strains (S. S. I and S. S. II) are known to be of the Shiga-Kruse variety, while two of the next four (S. A. I and S. A. II) are Flexner strains.

I was interested in finding that non-dysentery strains L. V and L. VI were both agglutinated in a dilution above 1:1,000 of serum L. V and serum L. VI. On checking them, I found that L. V and L. VI both came from the same patient and that, owing to an error in the spelling of the name, two stools from the same patient had been examined as coming from different ones.

SUMMARY.

1. In an epidemic of bacillary dysentery with a high death rate in Luzon, Province of Batangas, P. I., it has been shown that the Shiga-Kruse type of dysentery bacillus was the causative agent.
2. At the same time, the Flexner-Strong type of dysentery bacillus was found in some cases of dysentery around Manila.
3. The Bacillus Y and the Strong type with which Leutz worked were not found.
4. Great care is necessary in describing types of the dysentery bacillus from their reactions in sugar media alone, as the amount of sugar present and the length of time the organism has been on artificial media often affect the reaction.

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## PRACTICAL EXPERIENCES WITH BERIBERI AND UNPOLISHED RICE IN THE PHILIPPINES.<sup>1</sup>

By VICTOR G. HEISER.<sup>2</sup>

The advances made during the past year in placing the etiology of beriberi upon a scientific basis have now proceeded sufficiently to warrant the inference that prophylactic medicine has the knowledge at its command to place this scourge among the preventable diseases.

While it has been possible to control outbreaks of beriberi in public institutions in the Philippines during the past ten years by reducing the rice in the diet and replacing it with meat, vegetables, mongos,<sup>3</sup> etc., yet it was not until the papers which were read at the last annual meeting of the Far Eastern Association of Tropical Medicine, especially those of Fraser<sup>4</sup> and of Aron<sup>5</sup> gave the clue, that a rational method for the prevention and cure of the disease became available.

Briefly, it will be remembered that these gentlemen showed by experimental data that beriberi in man and polyneuritis in fowls could be caused by using as the staple article of diet, rice, from which the outer portion or pericarp had been removed, and that, unless advanced degeneration of the nerves had occurred an immediate amelioration of the symptoms took place when rice with the pericarp, or its equivalent, was substituted.

Numerous analyses of rice sold in the Manila market have been made by Aron, and these soon proved that Saigon rice number 2, as well as

<sup>1</sup>Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, February 23, 1911.

<sup>2</sup>Passed assistant surgeon, United States Public Health and Marine-Hospital Service; Director of Health for the Philippine Islands; and professor of hygiene, College of Physicians and Surgeons, University of the Philippines.

<sup>3</sup>A small bean, *Phaseolus radiatus* Linn. (*P. mungo* Blanco), similar to *katjang idjo* of Dutch East India. It has been proved by the native physicians of the Philippines as valuable as *katjang idjo* as a popular remedy for beriberi. According to the analysis of Aron (*This Journal*, Sec. B (1910), 5, 88) this bean contains 23.75 per cent protein; 9.56 per cent water; 0.77 per cent P<sub>2</sub>O<sub>5</sub>; 4.5 per cent fat; 6.4 per cent crude fiber.

<sup>4</sup>*Ibid.*, 55.

<sup>5</sup>*Ibid.*, 81.

locally polished rice, almost invariably contained less than 0.4 per cent of phosphorus pentoxide, unpolished or slightly polished rice was found to contain from 0.5 per cent to 0.75 per cent of phosphorus pentoxide.<sup>6</sup>

Since the opening of the Culion leper colony in 1906, rice has been the staple article of diet in the place, and it was customary to use either Saigon rice number 2, or local polished rice. Beriberi was more or less continuously present in the colony until February, 1910. By substituting meat and mongos for rice it was always possible to reduce the number of cases of beriberi, but the disease was never completely eradicated. It was found later that this failure was probably due to the fact that many of the lepers preferred to deny themselves food rather than to eat mongos, so that we had starvation as well as improper diet to deal with.

The total number of deaths at Culion by months from February, 1909, to February, 1910, among an average population of 1,537 was as follows: February, 39; March, 54; April, 52; May, 47; June, 48; July, 57; August, 61; September, 65; October, 43; November, 80; December, 188; January, 164; a total of 898. Of this number 309 were due to beriberi.

In February, 1910, the use of unpolished rice was made compulsory for all inmates of the Culion leper colony.

The total number of deaths for the months from February, 1910, to February, 1911, among an average population of 1,952, or a population greater by 27 per cent, was as follows: February, 66; March, 36; April, 29; May, 22; June, 27; July, 15; August, 24; September, 12; October, 13; November, 15; December, 58; January, 52; or a total of 369.

The increased death rate in December and January was due to an acute outbreak of bacillary dysentery. Of the number cited, there were no deaths from beriberi after February, 1910.

At the end of January, 1910, there were approximately 50 cases of beriberi undergoing treatment in the Culion hospital. Upon the suggestion of Doctor Aron, 30 grams of rice polishings mixed with milk and sugar were given to these patients twice daily. With the exception of two very advanced cases that died within a few days after this treatment was begun, all of them were able to leave the hospital, and within four weeks every case of beriberi was reported as cured by the attending physician of the hospital. So much for Culion.

Prior to May, 1910, beriberi was very common throughout the Philippines, in jails, light-house stations, charitable institutions, on Government vessels, and among the Philippine troops of the United States

<sup>6</sup> I wish to make clear that the amount of phosphorus in rice is only given because it is a ready method for determining the degree of polishing that a given rice has undergone; in other words, the estimation of the amount of phosphorus is a laboratory method of ascertaining whether much or little of the pericarp has been removed and at this time it can not be said that the lack of phosphorus causes beriberi.



Army. An investigation of these has shown that it was the invariable practice to use polished rice as the staple article of diet in all of the places mentioned. In May, 1910, an Executive Order was issued by the Governor-General of the Philippine Islands prohibiting the use of polished rice in all public civil institutions. Since August, 1910, only two cases of beriberi in the above places have come to the attention of the writer. One of these was among the crew of the steamer *Rizal*. An inspection of the ship's stores showed that the rice was of the white polished variety. Further inquiry elicited the fact that it was customary for the crew of this vessel to use a varied diet which may account for the fact that there were not more cases. The other case occurred in a prisoner in the jail at Tacloban. The physician in charge reported that it had not been possible to purchase unpolished rice at Tacloban and for that reason polished rice was being used. He added that every effort was, however, being made to comply with the spirit of the Executive Order by using more meat, mongos, potatoes, green vegetables, and fish.

At the Hospicio de San José, which is an insane and orphan asylum of over 700 inmates, beriberi has almost constantly been present, at least during the past ten years. Since June, 1910, unpolished rice has been used, and a few weeks after its use was begun beriberi disappeared, and since that time no further cases have been reported.

Extensive inquiry made throughout the Philippine Islands has almost invariably shown that in districts in which hand-pounded, or, in other words, unpolished rice, is commonly used, there is little if any beriberi, whereas in districts in which machined, or, in other words, polished rice, is served as the staple article of diet, beriberi is quite common. However, an apparent exception to this general rule is found among the residents of the Batanes Islands. It may perhaps be mentioned that these are isolated islands north of Luzon and south of Formosa, which have communication with the outer world only a few times each year, and, owing to their inaccessibility, they generally escape visitations of cholera and other dangerous communicable diseases.

The Batanes are poorly adapted to rice culture, and for this reason a considerable amount of polished rice is imported each year, and it would seem reasonable to infer that if the present theories with regard to the etiology of beriberi are correct, cases of this disease should be encountered in these islands. However, an investigation of the dietary of the inhabitants of the Batanes Islands shows that meat and potatoes are more commonly used than in other parts of the Philippines. In brief, food of various kinds, other than rice, is so plentiful that rice is not the staple article of diet to the same extent as elsewhere in the Archipelago.

Considerable difficulty has been encountered and much opposition has

resulted from the attempt to introduce unpolished rice. When the Army and the Insular Government entered the market to purchase large quantities, it developed that rice dealers were unable to supply the demand because managers of rice mills refused to adjust their process of manufacture to meet the new requirements. This resulted in the use of large quantities of rice that came from the mills immediately after it was husked. The machines that are employed locally for this purpose allow many of the smaller rice grains to pass through without the husks being removed from them. Previously such rice went directly to the polishing machine which not only polished the grains but the husks were also removed from such as still retained them, so that the finished product was clean. It was apparent then that much of unpolished rice which was issued in the beginning was not very clean and contained many husks. This gave rise to much complaint among those who were required to use it. It was frequently alleged that the husks tickled their throats and often caused gastritis. Upon investigation no reliable evidence as to the gastritis could be obtained. Commissary officers, prison wardens, and others who were directly charged with carrying out the orders to use unpolished rice were constantly besieged with complaints, and it was but natural that they should take the course of least resistance and recommend that its use be discontinued. To add to the difficulties of those who were insisting upon the use of unpolished rice, the rumor spread that the latter, when stored in bulk, soon spoiled, thus causing great financial loss. Investigation of this matter showed that there was no reason to believe that unpolished rice when stored under the same conditions as polished rice spoiled any more rapidly.

A campaign of education was then begun. Doctor Aron frequently went to the rice mills in person and was invariably able to demonstrate that rice could be rendered clean and free from husks without polishing it to a degree that would be harmful. Similar work, with like results, was accomplished by Highet in Siam, so that it may now be said that clean unpolished rice, satisfactory in appearance, can be obtained in the Philippines and abroad, and that the original objections to its use no longer exist.

By January, 1911, so much evidence had accumulated showing unpolished rice to be an important factor in the prevention of beriberi that it was deemed most desirable to bring about its general use in the Philippines for a few years at least, in order to test the theory thoroughly. At the most no harm can result, and upon the other hand every promise was held out that many hundreds of lives could be saved and a still greater morbidity avoided. Experimental investigations made by Doctor Aron showed that a rice which has only been polished to a point where it still contains 0.4 per cent of phosphorus pentoxide may be regarded as incapable of producing beriberi. Almost at the same

time similar conclusions were announced by Highet. Therefore, for purposes of convenience a rice containing less than 0.4 per cent of phosphorus pentoxide is regarded as polished and that which contains a greater percentage of phosphorus pentoxide as unpolished rice.

Accordingly, a bill was drafted which had for its purpose the bringing about of the general use of unpolished rice in those quarters where it furnished the staple article of diet. After considerable discussion with physicians, lawyers, legislators, and others, it was deemed advisable to attempt to secure the desired result by a law that would impose a tax of 5 centavos (2.5 cents United States currency) per kilogram upon all polished rice sold, whether it be foreign or domestic. However, owing to the fact that the Legislature adjourned during the early days of February, there was not sufficient time to present this matter to both Houses.

Because of the successful experience with unpolished rice in the prophylaxis of beriberi in the Philippines during the year, and since these data confirm the work of Fraser and Stanton,<sup>7</sup> Aron,<sup>8</sup> Kilbourne,<sup>9</sup> de Haan,<sup>10</sup> and Highet,<sup>11</sup> as reported at the last annual meeting of the Far Eastern Association of Tropical Medicine, it is believed that the time has come for the medical profession to aid in completing the last step in the test which promises so well to place another weapon in the hands of prophylactic medicine for the eradication of another of the world's serious and costly diseases.

<sup>7</sup> *Loc. cit.*

<sup>10</sup> *Ibid.*, 65.

<sup>8</sup> *Loc. cit.*

<sup>11</sup> *Ibid.*, 73.

<sup>9</sup> *This Journal, Sec. B* (1910), 5, 127.



## PERINEAL LITHOLAPAXY (KEITH'S OPERATION).

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By A. HOOTON.<sup>1</sup>

(*Rajkot, India.*)

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The trend of general surgical opinion, with reference to the treatment of stone in the urinary bladder, is, I suppose, more and more in favor of the employment of crushing operations in almost all cases in which they are practicable, and while admitting that very large stones usually are best dealt with by suprapubic lithotomy, and that certain cases associated with cystitis or suppuration about the neck of the bladder derive benefit from the drainage which is most easily afforded by a perineal lithotomy, I take it that everyone will agree that any safe procedure which enables litholapaxy to be applied to stones which would otherwise have to be removed by serious cutting operations is worthy of consideration. Keith's operation has this application, and it is with the view of bringing it to the notice of surgeons who perhaps may not previously have heard of it that this short account has been written.

It may first be noted that several procedures involving a combination of crushing with a larger or smaller incision in the perineum have from time to time been advocated by various authorities. Dolbeau was the first surgeon, so far as I am aware, to publish an account of such a combined operation, but his operation, which in essentials is that still described in the text-books under the name of perineal lithotomy or litholapaxy, differs from Keith's in the important fact that a much larger opening is made in the urethra to allow of the passage of large instruments designed merely to break up the calculus roughly, and not to crush it completely; and, indeed, it may be said that this method has more in common with lithotomy than litholapaxy pure and simple. Dolbeau's operation apparently was practiced intermittently by various surgeons for many years, but it was not until Dr. Keith of the Indian Medical Service introduced his modification that any large number of cases of crushing through a perineal incision were published, and that the operation—so changed in its details as to be practically new—acquired almost all the advantages of an uncomplicated litholapaxy. Dr. Keith, in his capacity of Civil Surgeon of Hyderabad, Scinde, with its five hundred cases of stone a year, had unrivaled opportunities of demonstrating the value of the procedure, and recorded a series of fifty-three cases in men, with three deaths, and one hundred and six cases in children, with no deaths. Surgeon-General Stevenson, Colonels W. H. Henderson and R. Baker, I. M. S., and other

<sup>1</sup> Major, I. M. S.

surgeons, have also employed Keith's method in the same hospital with most encouraging results, and Colonel Henderson has published a series of a hundred and ten cases with three deaths.

Keith's original operation in its turn has in recent years undergone further modification at the hands of various operators. Surgeon-General Stevenson, it would appear, makes a slightly larger opening so as to allow of one instrument being introduced alongside another, the principle being to retain a guide all the time; while Major S. Evans prefers to make his incision somewhat further back, and thus strike the wider prostatic portion of the urethra. Both these modifications would tend theoretically to minimize what I am convinced is the reason of the comparatively slow adoption of the operation by surgeons who have not had opportunities of seeing it actually performed, namely, the risk of missing the opening in the urethra in working without a guide. However, this risk is not a great one, for Keith's original incision strikes the urethra at a point where it is easily accessible, and where the wall, surrounded by the constrictor fibers, is more likely to grasp the instrument and so prevent leakage. In my experience it is not easy to work through a small opening using say the lithotrite as a guide for the canula to follow it; and, finally, the figures quoted above speak for themselves.

In the account given below, I have adhered closely to what I understand was Keith's original procedure, for any knowledge of which I wish to express my indebtedness to Colonel Henderson. I may remark that my own experience is limited to thirteen cases, all of which recovered. Those only which call for comment were three children with large stones, necessitating prolonged manipulation and the repeated passing of instruments, and in whom the small incision did not heal, as it ordinarily does, by first intention.

#### ADVANTAGES OF KEITH'S OPERATION.

A comparison may perhaps best be made with suprapubic lithotomy in adults, and lateral lithotomy in children and in both, perineal litholapaxy is usually, I would urge, very much preferable. Suprapubic lithotomy has, I think, a larger mortality, it necessitates prolonged confinement to bed, and the patient is a nuisance to himself and his attendants. Lateral lithotomy, although very successful in children, has all the disadvantages of involuntary micturition, and there is reason to believe that in some cases the sexual powers are interfered with.

In Keith's operation there is usually no shock, micturition is voluntary, the sexual apparatus is not injured, and the period of convalescence is usually not much longer than that of ordinary litholapaxy. I personally make a practice of keeping cases in for five to seven days, but often, after twenty-four hours, healing is so far advanced as to prevent any further escape of urine from the wound, and instances have frequently been noticed in which all urine escaped via the meatus from the first.

## INDICATIONS.

Various authorities recommend perineal litholapaxy under some or all of the following conditions:

- (1) A large or very hard stone necessitating the use of a lithotrite which will not pass easily by the natural route.
- (2) Stricture, in conjunction with a large or hard stone, or perhaps with any stone.
- (3) A difficult or narrow urethra.
- (4) Imperfect equipment—the absence of the smaller sizes of lithotrite.
- (5) Cases in which litholapaxy has been commenced in the ordinary way, but can not be completed satisfactorily owing to swelling of the urethra and deposit of débris.

## THE OPERATION.

Perineal litholapaxy may thus be performed: The patient is placed in the lithotomy position, and the thighs held so that the parts are as symmetrical as possible. A curved staff with a median groove is introduced into the bladder and held as in lithotomy, but neither drawn up beneath the pubes nor depressed. The scrotum is allowed to hang down in the natural position, and neither the operator nor the assistant steadies the skin.

A very small incision, or stab, is now made with the point of a tenotomy knife or double-edge scalpel, in children about one inch, in adults one and a half inches in front of the anus, through the median raphe in the direction of the staff; the groove is entered and the urethra incised for one-eighth inch or more and the knife withdrawn, slightly enlarging the superficial part of the incision as it emerges. The point of an ordinary director, which should not be too blunt, is inserted through the wound into the groove of the staff, and passed into the bladder; the staff is withdrawn, and graduated female sounds or Hegar's dilators introduced up to the required size. Some operators do not pass the dilators so far as the bladder, but there is at all events no harm in doing so.

Dilation is proceeded with slowly, and each instrument is left in position some little time; when the required aperture has been attained the director is withdrawn, leaving a circular, gaping orifice into the urethra. The appropriate size of evacuating catheter is now passed, and the bladder injected, and the lithotrite should follow without difficulty.

If preferred, the director can be guided into the groove of the staff along the knife, before the latter is withdrawn. Both cannula and lithotrite are entered point downwards, and carried into the bladder by the usual rotatory movement. The operation is completed in the same way as an ordinary litholapaxy, and as a rule there is no difficulty in retaining fluid in the bladder; if leakage should occur at the margins of the wound it is easy to compress them against the instrument.

In order to avoid a valvular aperture (which renders the introduction of instruments difficult) it is most important that the skin should not be displaced when making the incision. Also, it is better to enter the knife too far forward than too near the anus; in the latter case the instruments enter the urethra at an acute angle instead of vertically, and are much more likely to slip past the opening, and there is the added difficulty of working in a deeper wound. The chief danger of the operation lies in the lithotrite or cannula missing the urethral

opening, and passing upwards between the bladder and the rectum; the possibility of a small median wound of the bulb, especially in children, need not give rise to anxiety, and so far as I am aware, no cases of troublesome hæmorrhage have been recorded.

It is worthy of note that, contrary to what the anatomical text-books would lead one to expect, the most difficult part of a child's urethra, after the meatus, is often well in front of the membranous portion, so that an incision in the situation recommended almost always enables instruments of reasonable size to be passed.

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## A CLINICAL STUDY OF HOOKWORM INFECTION IN THE PHILIPPINES.<sup>1</sup>

By LIBORIO GOMEZ.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

The greater part of the work which has been done in relation to infections with hookworm has been statistical. Thus the publications of Garrison,<sup>(1)</sup> Rissler and Gomez,<sup>(2)</sup> Bowman,<sup>(3)</sup> and Willets<sup>(4)</sup> have established the varying percentages of infection in different parts of the Philippine Islands.

The investigation which is the subject of this paper was undertaken mainly to determine the effect of the hookworm on Filipinos and to determine whether there is any immunity enjoyed by the race, comparable to that of the Negros in Porto Rico, in the southern United States, and in Africa.

### MATERIAL AND METHODS.

A series of twenty-six cases was studied clinically, and subjected to a careful examination of the blood and urine.

The clinical examination included questions of the occurrence of previous diseases which would be likely to produce anæmia, such as tuberculosis, malaria, or dysentery, and queries as to present complaints. A close examination of the conjunctiva was also made because by this means the best evidence of pallor in dark-skinned people can be attained, and evidence was secured as to the presence of diseases of the lungs, heart, liver, spleen, stomach, and skin that are likely to produce eosinophilia.

The blood was examined for hæmoglobin by the Tallquist method and the erythrocytes and leucocytes estimated quantitatively. Wright's stain was used in the differential count of the leucocytes, from 300 to 800 leucocytes being counted in each case and care taken to examine the edges as well as the center of the smear.

The urine was tested for albumin by means of the heat acetic acid

<sup>1</sup>Read at the Eighth Annual Meeting of the Philippine Islands Medical Association, February 24, 1911.

and nitric acid methods, because the Anæmia Commission of Porto Rico<sup>(5)</sup> found that in many cases of hookworm infection albumin is present in the urine.

In a few cases the hookworms were collected and counted. It has been my procedure to collect the stools in every case. The patients were directed to pass all the stools in a vessel for twenty-four hours following the last purgative in the treatment, but considerable difficulty was experienced in making them comply with the instructions. Inasmuch as some worms may still be passed later than twenty-four hours after treatment, the number which I obtained may not represent the total number of parasites in every case, but the error can not be very great, as the number of hookworms recovered bears a very close relationship to the number of eggs found in a cover-glass preparation; it usually being about one to three.

Ten cases without hookworms but with other intestinal parasites were selected for study as controls.

#### DISCUSSION OF FINDINGS.

As is shown in the table, five cases out of twenty-six complained of a certain amount of pain in the stomach. The other symptoms, such as emaciation, a feeling of dizziness, pain in the joints, difficulty in urination, a sensation of oppression on the chest, tympanitis, neuralgic intercostal pains, or debility, can be attributed to other diseases such as malaria, tuberculosis, dengue fever, cystitis, and nephritis.

The vague pains in the stomach suggest the presence of hookworms, either alone or associated with other intestinal parasites, as their removal is followed by immediate relief. Pain in the gastric region as a symptom accompanying hookworm infection has been frequently observed by Doctor Rissler and me in our work in Rizal and Cavite Provinces and the Cagayan Valley. One particular instance was that of our own assistant in Las Piñas, Rizal, who complained of poor appetite and vague abdominal pains, and who was promptly relieved on the expulsion of hookworms. The occurrence of vague digestive and abdominal symptoms is also mentioned by Bass<sup>(7)</sup> in connection with mild infections with hookworm in the southern United States. The reference of the pain to the stomach and abdominal region may be explained by the anatomic arrangement of the sympathetic innervation of the duodenum which is connected, through the solar plexus, with the remainder of the abdominal organs, and particularly with the stomach.

As compared with the control cases, eosinophilia is generally present in the patients harboring hookworms. Five out of 10, or 50 per cent, of the control cases gave an eosinophile count above 4 per cent. In patients infected with hookworm, 20 out of 26, or 76 per cent, had eosinophiles above 4 per cent. Only 3 of the controls had over 5 per

cent, whereas in the hookworm series, this figure was reached by 20 out of 26 of the cases. No control shows 13 per cent or above, whereas 9 (or 34 per cent) of the cases harboring hookworms gave an eosinophile count of 13 per cent or above. The lowest count in the control cases was 0.3 per cent, and the highest 12.80, whereas in the others the lowest was 0.3 per cent and the highest 21.9. It is to be noted in the control series that individuals with *Trichuris* or *Ascaris*, or both together, hardly show any deviation from normal (0.5 to 4.00 per cent, Cabot), those having high eosinophile counts harbored amœbæ or *Tænia*. Chamberlain<sup>(6)</sup> in his work on light infection with *uncinaria* among southern-bred white soldiers found eosinophilia to be present in the majority of cases, the lowest count being 1 per cent and the highest 26.

The percentage of hæmoglobin in the control series varied from 80 to 95. In the cases infected with hookworms, the percentage was from 75 to 95. The count of the red and white cells does not show any marked difference between the two series; the lowest for red cells in the hookworm cases is 4,000,000 per cubic centimeter whereas in the control cases it was 4,500,000.

In two instances (3 and 12), albumin was found in the urine but this occurrence can be attributed to nephritis which was independent of the hookworm infection.

The number of hookworms recovered varied from 1 to 20, this small number corresponding to the paucity of eggs found in the microscopic preparations.

One case has been followed closely:

*Case 17.*—N. S., age 23, from Gerona, Tarlac. Patient previously was a clerk. Examination of the fæces, April 13, 1910, ova of *Ascaris*, *Trichuris* and hookworm were found.

*Previous diseases.*—No tuberculosis, no malaria.

*Present complaint.*—The only complaint is fleeting pains in the gastric region, about one and one-half inches to the left of the median line at the level of the costal border. This pain existed for more than three years and occurs especially in the morning when the patient's feet are bare and cold. The pain is dull and when it occurs there is simultaneously the appearance of thin watery saliva. This condition lasts from one to three days and is repeated several times a month. It has no connection with the patient's food.

*Physical examination.*—The conjunctiva are of good color, the tongue not coated, plantar surface not fissured. No murmur in heart, slight accentuation of the pulmonic second sound.

*Blood examination.*—Hæmoglobin 85 per cent, erythrocytes 5,580,000, leucocytes 6,000, polymorphonuclears 26 per cent, small mononuclears 35 per cent, large mononuclears 9 per cent, eosinophiles 20 per cent.

Two weeks after treatment the patient was interrogated concerning his pain and he said it had entirely disappeared. A month later leucocytes were examined with the following results: Polymorphonuclears 43.4 per cent, small mononuclears 36.2 per cent, large mononuclears 6.1

per cent, eosinophiles 14.1 per cent. The faeces were negative for ova of the hookworm.

The eosinophilia is possibly due to a toxin secreted by the worm. According to Ashford and King<sup>(8)</sup> this was isolated by Lussano by evaporating at a temperature of 60° to 70° the urine of a patient infected with hookworms until it became sirupy, then extracting with absolute alcohol and dissolving the extract in distilled water. He made subcutaneous injections of this supposed toxin into rabbits continuously for eight days, causing a diminution in the number of red cells, poikilocytosis and rapid formation of fibrin, all of which symptoms disappeared upon the cessation of the injections. The parasites were then expelled from the patient and a similar preparation from the urine afterwards had no effect.

Bohland<sup>(9)</sup> also believed a breaking down of the body albumin to occur, due to a poison.

The persistence of eosinophilia after the removal of the worms is explained by Leichtenstern<sup>2</sup> as a result of the hypertrophy of that portion of the bone marrow concerned in the production of eosinophiles.

The comparative absence of clinical symptoms in hookworm infections in the Philippines probably does not mean the presence of racial immunity among the Filipinos, as the infecting organisms are few. According to Thornhill,<sup>3</sup> there must at least be 500 present for from six months to one year, in order to produce such symptoms, and other patients may develop anaemia and debility as a result of only from 100 to 300 parasites.

In Porto Rico, where the disease is evident clinically, Ashford and King<sup>(12)</sup> counted the number of hookworms expelled from twenty-two patients with the following results: In 9 cases there were less than 300 worms, in 8 cases between 300 and 1,000, in 3 cases between 1,000 and 2,000, in 1 case 2,749 and in another 4,397 hookworms. Therefore, the disease in the Philippines corresponds to the light type of Stiles,<sup>(13)</sup> in which the patients show ova in the stools, but do not exhibit any, or sufficiently marked, symptoms to attract especial attention.

#### CONCLUSIONS.

1. The most frequent and only subjective symptoms in these cases of uncinariasis occurring alone or in association with other intestinal parasites were vague abdominal pains and loss of appetite.

2. Eosinophilia was found in a majority of cases, the lowest eosinophile count being 0.3 per cent, the highest 21.90 per cent.

3. Hookworm infection among the Filipinos corresponds to the light type of Stiles, that is, patients have the ova of hookworms in their stools, but no symptoms.

<sup>2</sup> Cited by Boycott and Haldane.<sup>(10)</sup>

<sup>3</sup> Cited by Scheube.<sup>(11)</sup>

4. The absence of all clinical manifestations or their insignificant characters among Filipinos infected with hookworms can not be attributed to a racial immunity, as the number of the infecting hookworm organisms in each instance is small.

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TABLE I.—Cases of

No. of case.	Date.	Prison number.	Age.	Previous residence.	Previous employment.	Examination of feces.	Previous diseases.	Present complaint.
	1910.							
1	Mar. 7	8356	21	-----	Scout soldier.	Hookworm, <i>Trichuris</i> .	Negative	None
2	Mar. 7	18592	16	-----	Messenger.	do	do	do
3	Mar. 8	7979	40	Naguilian, Union.	Laborer in rice and tobacco fields.	do	Rheumatism.	Frequent epigastric pain.
4	Mar. 12	-----	28	Manila	Employee in the prison.	Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	Cough	Emaciation
5	Mar. 14	7994	24	do	Clerk	do	Negative	Vertigo for about a year.
6	Mar. 14	8376	35	-----	Laborer in rice paddies.	do	Malaria two years ago.	None
7	Mar. 15	8001	18	-----	do	Hookworm	Negative	do
8	Mar. 15	7995	21	-----	Laborer	do	do	do
9	Mar. 15	8003	17	-----	Laborer on abaca.	do	do	do
10	Mar. 29	18841	20	Luzuriaga, Occidental Negros.	do	Hookworm, <i>Ascaris</i> .	Indefinite fever.	Pain in joints but no fever.
11	Mar. 29	8410	23	Malolos, Bulacan.	Laborer in rice paddies.	Hookworm	Negative	None
12	Mar. 29	8028	56	Indang, Camarines.	do	do	do	Coughs; does not urinate freely; pain in pubic region; breath short when tired.
13	Mar. 29	8407	20	Calumpit, Bulacan.	do	do	Rheumatism.	None
14	Mar. 29	8408	18	do	do	Hookworm, <i>Ascaris</i> .	do	Pain in the epigastrium frequently.

*hookworm infection.*

Physical examination.	Hæmoglobin cent.	Examination of the blood.							Albumin in urine.	Number of hook-worms recovered.
		Erythrocytes.	Leucocytes.	Polymorpho-nuclears.	Mononuclears.		Eosinophiles.	Basophiles.		
					Small.	Large.				
Negative -----	85			47	28	6	18	0.4	N e g a - t i v e .	} = 15
Eczema of nates, months' duration.	75			67	16	6	9		do -----	
Negative -----	80	4,000,000	7,500	57.30	18.70	4.90	19.10	0.3	Positive	
do -----	85	4,500,000	4,800	57	39	3	0.3		N e g a - t i v e .	
do -----	85	4,920,000	5,600	79	14	4	3		do -----	
do -----	90	4,480,000	4,800	60	20	11	9		do -----	15
do -----	85	4,540,000	9,240	54	26	7	13		do -----	20
Sluggish reflexes.	75	4,880,000	4,600	60	34	3	3		do -----	12
Negative -----	75	4,600,000	7,000	62	16	8	14		do -----	14
Pale conjunctiva; coated tongue; tenderness in epigastrium.	90	5,200,000	6,960	63	21	5	10		do -----	6
Negative -----	90	5,500,000	11,550	67	17	5	13		do -----	
Slightly pale conjunctiva; tongue coated; bronchial breathing.	85	4,420,000	7,000	66	25	6	3		Positive	17
Negative -----	90	5,400,000	6,600	62	26	8	3	0.3	N e g a - t i v e .	
Slightly pale conjunctiva.	90	5,700,000	5,940	65	28	6	2		do -----	

<sup>a</sup> Cases 1 and 2 had hookworms collected together.

TABLE I.—Cases of

No of case.	Date.	Prison number.	Age.	Previous residence.	Previous employment.	Examination of fæces.	Previous diseases.	Present complaint.
15	Apr. 13	8452	25	Victoria, Gerona, Tarlac.	Laborer in rice paddies.	Hookworm.	Rheumatism.	Feeling oppression in chest at times.
16	Apr. 13	8457	27	do	Merchant.	Hookworm, <i>Ascaris</i> .	do	Occasional tympanitis.
17	Apr. 13	8456	23	do	Clerk	Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	do	Fleeting dull epigastric pains.
18	Apr. 20	6914	23	Santo Tomas, Batangas.	Merchant.	Hookworm, <i>Ascaris</i> , <i>Amoeba</i> , <i>Trichuris</i> .	do	Pain in abdomen about umbilical region occasionally; no appetite.
19	Apr. 26	8073	20	Caloocan, Rizal.		Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	do	Neuralgic intercostal, and cephalic pains.
20	Apr. 27	19102	21	Bautista, Pangasinan.	Mechanic	do	Cough; pain in chest.	None
21	Apr. 28	12112	18	Manila	Messenger.	Hookworm.	Negative	Vertigo
22	Apr. 88	19110	22	Luna, Union	Laborer in rice paddies.	do	Malarial fever.	None
23	May 12	8109	26	Sinay, Ilocos Sur.	Tailor	do	Spat blood	do
24	May 16	19278	24	Pandan Candatuan, Albay.	Laborer on abaca.	Hookworm, <i>Ascaris</i> , <i>Trichuris</i> .	Spat blood; dysentery, malaria.	Debility
25	May 16	8550	65	Albay, Albay.	Laborer	do	Negative	None
26	May—	19300	18	Manila	Clerk	do	Spat blood	After meals he has pain on left side of abdomen.



*hookworm infection*—Continued.

Physical examination.	Hæmoglobin per cent.	Examination of the blood.							Albumin in urine.	Number of hookworms recovered.
		Erythrocytes.	Leucocytes.	Polymorpho-nuclears.	Mononuclears.		Eosinophiles.	Basophiles.		
					Small.	Large.				
Conjunctiva slightly pale; tongue coated; fissuring plantar surface.	80	5,200,000	8,000	64	20	8	8	-----	Negative.	1
Conjunctiva pale; tongue coated.	85	5,640,000	10,200	55	26	6	13	-----do-----		5
Slight accentuation of second pulmonic sound.	85	5,580,000	6,000	36	35	9	20	-----do-----		b
Tongue coated	90	5,200,000	6,600	58	21	7	14	-----do-----		17
Negative	90	-----	-----	55.43	29.89	6.52	8.42	-----do-----		5
do	90	-----	-----	35.35	36.67	5.53	21.90	0.50 do		
do	90	-----	-----	57	27	8	7	0.3 do		1
Slightly pale conjunctiva.	85	-----	-----	68	16	7	8	0.2 do		
Negative	90	-----	-----	60.35	21.11	5.19	13.33	-----do-----		
Slight dullness left apex; tenderness over epigastrium.	90	-----	-----	47.38	19.92	9.47	23.01	0.19 do		6
Tongue coated; conjunctiva rather pale.	90	-----	-----	55.77	30.48	7.24	6.59	0.18 do		10
Negative except some herpetic eruption.	95	-----	-----	58.79	28.51	11.91	5.23	0.54 do		

<sup>b</sup> Stool not collected.

TABLE II.—Control

No. of case.	Date	Prison number.	Age.	Previous residence.	Previous employment.	Examination of fæces.	Previous diseases.	Present complaint.
1	1910. Mar. 28	18833	50	Namakpan, La Union.	Laborer on tobacco.	<i>Trichuris</i> , <i>Ascaris</i> .	Malaria a year ago.	Pain in back.
2	Mar. 28	18830	35	Lawag, Ilocos Norte.	Tailor	<i>Ascaris</i>	Opium smoker; spat blood.	None
3	Mar. 29	18834	36	Naguilian Union.	Tobacco merchant.	do	Spat blood in 1907; fever a few days ago.	Pain in chest occasionally.
4	Mar. 30	18850	27	Manila	Clerk	<i>Trichuris</i>	Negative	None
5	Mar. 30	18851	79	do	Banquero	do	do	do
6	May 13	8104	24	Bangued, Abra.	Carpenter	<i>Amœbæ</i>	Pain in chest and back; bloody stools.	Bloody stools.
7	May 13	8108	27	Narvacan, Ilocos Sur.	Clerk	<i>Tænia</i>	Has had headache frequently.	Headache, pain in abdominal region and back; difficulty in urination.
8	May 16	19279	18	Guinobatan, Albay.	Laborer on abaca.	<i>Trichuris</i> , <i>Ascaris</i> , <i>Amœbæ</i> .	Malaria; dysentery with mucus and blood.	Pain in epigastrium.
9	May 16	8113				<i>Ascaris</i>		
10	Mar. 28	6004				<i>Amœbæ</i> , Monads.	Malaria; chronic bronchitis.	None

cases.

Physical examination.	Hæmoglobin, per cent.	Examination of the blood.							Examina- tion of urine for albumin.
		Erythro- cytes.	Leucocytes.	Polymorpho- nuclears.	Mononuclears.		Eosino- philes.	Basophiles.	
					Small.	Large.			
Negative -----	85	5,020,000	8,600	70	18	7	5		Negative.
do -----	90	5,420,000	5,600	63	32	5	0.3	0.7	Do.
do -----	95	6,000,000	6,800	63	27	9	1		Do.
do -----	90	5,200,000	10,000	69.6	20.1	6	4.2		Do.
do -----	90	4,800,000	5,400	70	20	6	4		Do.
do -----	90			52.50	27.69	7.11	12.69		Do.
do -----	90			58.75	26.04	5.64	10.54		Positive.
Tongue coated; conjunctiva slightly pale; some fissuring of the feet.	90			67.19	11.93	8.07	12.80		Negative.
do -----	95			69.49	18.64	9.33	2.3		Do.
Negative -----	80	5,500,000	8,500	67	21.00	8	4		Do.



## A CONTRIBUTION TO THE ETIOLOGY OF BERIBERI.<sup>1</sup>

By WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.<sup>2</sup>

(From United States Army Board for Study of Tropical Diseases.)

In the *Lancet* for December 17, 1910, Fraser and Stanton report a series of experiments in which they prove that 85 per cent of the phosphorus contained in rice polishings is negligible in the prevention of polyneuritis of fowls. Their method of experiment is briefly as follows:

One hundred grams of rice polishings, containing 4.1 grams phosphorus pentoxide were extracted with 0.3 per cent hydrochloric acid solution which dissolved out 3.6 grams or 88 per cent of the phosphorus. They then added a sufficient quantity of alcohol to precipitate all the phytin contained in the solution which amounted to 3 grams or 73 per cent of the total phosphorus. The phytin was filtered out and the filtrate contained only 0.6 gram, or 15 per cent of the total phosphorus originally present in polishings.

They then fed one series of fowls on polished rice plus the phytin containing 73 per cent of the phosphorus and another series of fowls on polished rice plus the filtrate containing only 15 per cent of the phosphorus. The fowls receiving the phytin developed neuritis while those receiving the filtrate remained in good health. This proved that 85 per cent of the total phosphorus content (73 per cent contained in the phytin and 12 per cent which remained in the polishings) is unimportant in preventing polyneuritis gallinarum.

We have repeated this work done by Fraser and Stanton and are able to confirm their results. We fed three fowls on polished rice alone and three others on polished rice plus the filtrate prepared according to their method, with the result that the three fowls receiving only polished rice developed neuritis in 18, 30, and 43 days, respectively, while of the fowls fed on polished rice plus the filtrate one died at the end of 58 days of avian diphtheria without ever showing signs of neuritis, and the other two lived until the 73d day in good health, at the end of which time the experiment was concluded.

<sup>1</sup>Published with permission of the chief surgeon, Philippines Division.

<sup>2</sup>W. P. Chamberlain, major, Medical Corps, United States Army, and Edward B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

This strikes a hard blow at the idea that the lack of phosphorus compounds is the cause of beriberi or polyneuritis gallinarum.<sup>3</sup> However, there is still a possibility that the remaining 15 per cent of phosphorus in some particular combination is the important element. We believe that our work disposes of even this possibility, and that, as a result, the idea that multiple neuritis of fowls is due to a deficiency of phosphorus compounds must be abandoned.

Our first step was to analyze this filtrate of Fraser and Stanton for inorganic constituents, and we found that it contained 0.18583 per cent magnesium phosphate and 0.01766 per cent of potassium phosphate.

In a previous paper from this laboratory Kilbourne<sup>(1)</sup> had suggested the possibility that potassium salts might bear some relation to the production of beriberi and subsequently an attempt was made by this Board<sup>(5)</sup> to settle the point by feeding one group of fowls on polished rice plus potassium chloride, another groups on polished rice plus phosphoric acid, and a third group on polished rice with the addition of both potassium chloride and phosphoric acid. These experiments were completely negative and the fowls receiving these substances developed neuritis as promptly as fowls receiving polished rice alone.

In spite of these discouraging results and the statement by Schaumann<sup>(2)</sup> that the inorganic salts can have nothing to do with the prevention of neuritis, we determined to give these salts a more thorough trial for the following reasons: First, we had demonstrated the presence of magnesium and potassium phosphate in an extract that was proved to prevent neuritis, and, therefore, even if these salts gave negative results, their elimination would further simplify the problem and would prove that a part at least of the 15 per cent of phosphorus found in the filtrate of Fraser and Stanton was not concerned in the prevention of neuritis of fowls. Second, we had observed in various analyses of rices and rice polishings that the potassium content varied in the same manner as the phosphorus content and appeared to be just as good an *index* of its neuritis-preventing or neuritis-producing power.

The following experiment was performed for this purpose. Four groups of fowls, each group consisting of four birds, were fed on polished rice. In addition, Group A received daily 0.07 gram of potassium phosphate; Group B received 0.07 gram potassium citrate; Group C received 0.07 gram potassium carbonate and Group D received 0.07 gram magnesium phosphate. These salts were administered in the dose of 0.07 gram because analyses showed that this amount was

<sup>3</sup>The view that phosphorus was the essential neuritis-preventing element has been especially advocated by Schaumann<sup>(2)</sup> but not by Fraser and Stanton who were particular in stating that the amount of phosphorus pentoxide was only an *indicator* of the neuritis-producing power<sup>(3)</sup> of the grain.

slightly greater than the quantity of potassium in five grams of polishings, which latter quantity is known to be sufficient to maintain fowls in health. In order to facilitate administration 7 grams of each of these salts except the magnesium phosphate were dissolved in 100 cubic centimeters of distilled water. The magnesium phosphate being insoluble was simply suspended in water in the proportion 7 grams to 100 cubic centimeters. One cubic centimeter of these solutions and the suspension was administered daily to each fowl with a pipette. Therefore there can be no doubt as to what each fowl actually received. We might state at this point that this method of administration has been employed in all of our experiments.

The result of this series of experiments is briefly as follows:

*Group A* (receiving potassium phosphate): One fowl developed neuritis in 22 days and one in 24 days.

*Group B* (receiving potassium citrate): One fowl developed neuritis in 22 days and one in 24 days.

*Group C* (receiving potassium carbonate): One fowl developed neuritis in 21 days and one in 23 days.

*Group D* (receiving magnesium phosphate): Two fowls developed neuritis on the 24th day.

The experiment was discontinued on the 28th day since it was considered amply demonstrated that none of these salts conferred any protection.

We may draw several conclusions from this experiment.

1. Lack of potassium as a cause of polyneuritis can probably be excluded, because we have tried four salts of this element, one of them known to be present in rice polishings and one of them being the salt of an organic acid, and all of these salts of potassium signally failed to confer protection.

2. Magnesium phosphate, a salt present in considerable quantity in the filtrate of Fraser and Stanton, is also shown to be of no value. This probably excludes the element magnesium from further consideration.

3. By a rough calculation the phosphorus contained in the magnesium and potassium phosphate of the filtrate of Fraser and Stanton which we prepared is equivalent to about one-fifth of the 15 per cent of total phosphorus remaining according to their analyses. Since we have shown that these salts are unimportant we can state at this point that 88 per cent of the total phosphorus of rice polishings is negligible. We have not given all the figures for the sake of brevity and because our results by the method which follows are so conclusive as to the unimportance of phosphorus compounds.

Fraser and Stanton<sup>(3)</sup> have shown that the neuritis-preventing principle of rice is soluble in hot alcohol and Hulshoff-Pol<sup>(4)</sup> proved that a decoction of *katjang idjo* (*Phaseolus radiatus*) has the same curative

and preventive power as the beans themselves, so that the neuritis-preventing principle of these legumes is evidently soluble in hot water. Our work, detailed below, has shown that the active neuritis-preventing principle of rice polishings is soluble in both cold alcohol and cold water.

*Experiment 1.*—One kilogram of rice polishings was mixed with about 3,000 cubic centimeters of water and allowed to macerate over night. The resultant mixture was filtered carefully after extraction had proceeded for 24 hours. Two thousand cubic centimeters of a deep yellow liquid was obtained.

Four fowls were now fed on polished rice and given daily 20 cubic centimeters of this filtrate. In this way the fowls received the substances extracted by cold water from 10 grams of polishings. After the experiment had proceeded for several weeks and the fowls appeared to remain in health the dose of the extract was reduced to 10 cubic centimeters. These four fowls all remained healthy for 70 days at the end of which period the experiment was discontinued.

The neuritis-preventing principle of rice polishings is therefore soluble in cold distilled water.

*Experiment 2.*—One kilogram of rice polishings was mixed with 3,000 cubic centimeters 95 per cent alcohol. After macerating for 24 hours, the resultant fluid was filtered, the filtrate being a perfectly clear, light green liquid. The polishings were expressed in a towel to obtain the whole of the fluid. This clear alcoholic extract was placed in a water bath on which an electric fan was turned. The alcohol was evaporated rapidly by this method without much rise in temperature. When the alcohol had all disappeared the remaining liquid was placed in a separating funnel and after standing for about half an hour, there was a clear separation into two layers. The upper and larger layer was a deep green in color and contained all the fat extracted by this method. The lower and smaller layer was brown in color and was a thick, sirupy liquid. By carefully pouring distilled water into the funnel the separation of these two layers was rendered easier, since the water lay in a third layer below the fats but above the brown liquid. The lower layer of brown sirupy liquid was then drawn off. The fat was discarded, since it has repeatedly been shown that the fat of rice polishing has nothing to do with the prevention of neuritis. The lower layer therefore contained all the substances that were dissolved out of the polishings by cold alcohol except the fats. About 25 cubic centimeters of this extracted material was obtained from 1 kilogram of polishings and was then mixed with 1,000 cubic centimeters of distilled water, when a precipitate was formed consisting of those substances, other than the fats, that are soluble in alcohol but not in water.



Four fowls were then fed on polished rice giving them a daily dose of 10 cubic centimeters of this cloudy fluid representing the substances, other than fat, dissolved by alcohol from 10 grams of polishings. Of these four fowls, one died on the 69th day, probably of avian diphtheria, without ever showing any signs of neuritis, and the other three remained in good health until the 70th day, when the experiment was discontinued.

Therefore, the neuritis-preventing principle is soluble in cold 95 per cent alcohol.

Since the neuritis-preventing principle of rice polishings is soluble in both cold water and cold alcohol, it is apparent that by combining these two solvents the resultant extract can be much simplified, because certain substances derived from the polishings are soluble in alcohol but not in water, and vice versa. This is the principle that was adopted in the following experiment.

*Experiment 3.*—The cloudy extract used in experiment 2 was filtered until a perfectly clear yellowish fluid was obtained. This fluid contained only those substances extracted from rice polishings by alcohol and soluble both in alcohol and water.

Four fowls were fed on polished rice, with a daily dose of 10 cubic centimeters of this clear extract. These four fowls lived for 70 days in good health, thereby proving that this extract is capable of preventing neuritis, since in our experience fowls fed on polished rice alone developed neuritis in about 30 days on the average.

Through the courtesy of the Bureau of Science<sup>4</sup> the extracts used in these experiments were analyzed with the following result:

The precipitate which had not been removed from the extract used in experiment 2, but had been removed from the extract given to fowls in experiment 3, contained 0.000033 per cent phosphorus pentoxide and 0.00116 per cent nitrogen.

The clear filtrate given to fowls in experiment 3, contained 0.00165 per cent phosphorus pentoxide and 0.0406 per cent nitrogen.

It will readily be seen that the fowls in experiment 2 received the sum of the phosphorus and nitrogenous substances contained in the precipitate and filtrate. In both experiments the amount of phosphorus received was so small as to be negligible. One hundred cubic centimeters of the filtrate used in experiment 3 contained only 1.6 milligrams of phosphorus pentoxide and since the daily dose given the fowls was 10 cubic centimeters they received 0.16 milligram phosphorus pentoxide daily, whereas if they had been fed 10 grams of rice polishings they would have received from 200 to 500 milligrams of phosphorus pentoxide. The total amount of phosphorus pentoxide in rice polishings

<sup>4</sup>We hereby desire to express our obligation to Mr. Harry D. Gibbs, Dr. A. P. West, and Mr. R. R. Williams, chemists of the Bureau of Science, who independently performed these analyses.

varies from 2 to 5 per cent so that a brief calculation will show that the extract prepared according to this method contains between 1/1,000 and 1/5,000 of the total amount of phosphorus contained in the original polishings. In other words, at least 999 parts out of each 1,000 parts of phosphorus are proven to be unimportant in the prevention of polyneuritis of fowls. It is impossible to state positively that this minute trace of phosphorus remaining in the extract is not the neuritis-preventing element, but we can at least say that it appears utterly incredible that it can be of the slightest importance. Therefore, the theory, especially advocated by Schaumann,<sup>(2)</sup> that beriberi and polyneuritis gallinarum are caused by a lack of phosphorus compounds, is strongly discredited to say the least.

However, these findings do not necessarily conflict with the statement made by Fraser and Stanton<sup>(3)</sup> and by others, including this Board, to the effect that the proportion of phosphorus pentoxide present in a rice is an *index* of its beriberi-preventing powers. Such a statement has never, so far as we are aware, been intended to convey the impression that beriberi was due to a lack of phosphorus compounds, but merely means that a rice containing phosphorus in amounts above 0.4 per cent phosphorus pentoxide necessarily has a sufficient quantity of pericarp adhering to the kernel; i. e., it is sufficiently undermilled. As shown by a former publication of the board<sup>(5)</sup> the presence of a certain percentage of potassium appears to be an equally reliable index of safety, and so in fact would be presence in a rice of a definite percentage of any substance which is found exclusively or almost exclusively in the pericarp and the aleurone layer.

The 0.0406 per cent of nitrogen contained in this extract would indicate a considerable quantity of proteid matter provided the nitrogen were present in combination with proteids. This would not seem to be the case, however, since the extract failed to give the xanthoproteic and biuret reactions and moreover we should not expect to find proteids in a fluid obtained by extracting with alcohol, but in order to prove this point we determined to test the extract by the method of dialysis.

*Experiment 4.*—The brown residue obtained from 2 kilograms of rice polishings, macerated with cold alcohol according to the method described above in experiment 2, was mixed with 300 cubic centimeters of distilled water and filtered until clear. This small bulk of water was used in order that the aqueous extract resulting might be quite concentrated. This aqueous extract, which contained only those substances soluble in cold water and cold alcohol, was then placed in a parchment bag and suspended in distilled water. This parchment was previously tested with solutions of egg albumen and sodium chloride, and it was found that the sodium chloride passed freely through the membrane while the egg albumen did not pass through at all. During the process of dialysis the apparatus was kept in the ice-box to prevent decomposition of the extract. At the end of two days, when the fluid on the outside of the bag had become a deep yellow, the diffusate was

removed and the apparatus refilled with distilled water. This process was repeated three times, and the combined fluid removed from the outside of the bag, containing all the diffusate, was brought to 1,000 cubic centimeters, while the extract remaining inside the bag, the dialysate, was diluted likewise to 1,000 cubic centimeters.

Four fowls were now fed on polished rice plus 10 cubic centimeters daily of the dialysate and four other fowls were also fed on polished rice plus 10 cubic centimeters daily of the diffusate, with the following results.

*Group 1* (four fowls receiving polished rice plus dialysate): One fowl died of inanition in 23 days. One fowl developed neuritis in 38 days, one in 42 days and one in 52 days.<sup>5</sup>

*Group 2* (four fowls receiving rice plus diffusate): All four remained well at the end of 70 days.

Therefore, it is apparent that the neuritis-preventing substance is capable of dialyzing through a parchment membrane.

Analysis of this diffusate showed that it contained only 0.02 per cent nitrogen so that at least half of the nitrogen originally present must have been combined in some other form than proteid, because there could be no proteid present in the diffusate.

The results of this last experiment are very far-reaching in their importance. Since the neuritis-preventing substance can dialyze through a parchment membrane it must belong to the class of crystalloids, and all colloidal substances, including proteids, gums, starches, dextrans, and many other substances, may be eliminated from further consideration. Probably enzymes also can be excluded.<sup>(6)</sup>

#### CONCLUSIONS.

1. Polyneuritis gallinarum is not prevented by adding to a diet of polished rice any of the following substances; potassium phosphate, potassium citrate, potassium carbonate, potassium chloride, magnesium phosphate, phytin, phosphoric acid, or phosphoric acid combined with potassium chloride.

2. The neuritis-preventing substance in rice polishings is soluble in cold water and in cold alcohol.

3. Polyneuritis gallinarum may be prevented by means of an extract of rice polishings containing only those substances soluble in cold water

<sup>5</sup>The rather long "incubation period" for the neuritis in this group we believe to be due to the fact that the first supply of dialysate fed to these fowls was prepared not in a bag (as described above), but in a bottle with the mouth covered with parchment. The small dialyzing surface probably rendered dialysis slow, allowing a part of the neuritis-preventing substance to remain behind and thereby delaying the onset of the disease.

and cold alcohol. This extract, so far as at present known, has the following composition:

	Per cent.
Total solids	1.34
Ash	0.03
Phosphorus pentoxide	0.00165
Nitrogen	0.0406
Sucrose	0.88

4. Multiple neuritis in fowls fed on polished rice probably is not due to lack of phosphorus compounds in the grain, as claimed by Schaumann, since out of each 1,000 parts of phosphorus contained in the rice polishings at least 999 are not concerned in preventing neuritis.

5. The neuritis-preventing substance contained in rice polishings is capable of dialysis through a parchment membrane. This excludes all colloids from consideration.

We realize that the above conclusions are based on a small series of experiments, but the results appear so conclusive and are so far-reaching in their importance that it is deemed desirable to report them at once. Further experiments are now under way to confirm the above observations and also to determine the effect on fowls of the remaining untried substances contained in this extract, including the sucrose which it will be observed constitutes much the larger part of the total solids.

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A COMPARATIVE STUDY OF THE AMOEBÆ IN THE  
MANILA WATER SUPPLY, IN THE INTESTINAL  
TRACT OF HEALTHY PERSONS, AND IN  
AMOEBIC DYSENTERY.

---

By ERNEST LINWOOD WALKER.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

---

The etiologic relation of amœbæ to endemic dysentery, while not established upon all of the postulates of Koch, is supported by clinical, pathologic, and experimental evidence and has become generally accepted; but, notwithstanding the attention these parasites have received in recent years, investigators are not agreed upon how many species are parasitic in the intestinal tract of man, whether they are obligatory parasites or whether amœbæ from water or other external sources are capable of colonizing in the human intestine, their cultivability on artificial media, and the species concerned in the production of amœbic dysentery.

The importance of these questions at issue is evident. They concern not only clinical and preventive medicine, but involve important financial considerations as well. The correct microscopic diagnosis of, and the application of early treatment to, amœbic dysentery depends upon our ability to identify the pathogenic amœba; and the requirement for radically different prophylactic measures as well as the necessity for large expenditures to distil, filter, or otherwise treat water from uncontaminated supplies in the Tropics so as to kill or remove the amœbæ which such water always contains depend upon whether or not the pathogenic amœba is an obligatory parasite.

The problem is primarily one of species, of the identity of the amœbæ that have been described by different authors in water, in cultures, in stools of healthy persons, and in amœbic dysentery. Anyone who has attempted to identify amœbæ by the descriptions in the literature will probably admit that species determination of the Amœbidæ is in a chaotic state. New species have repeatedly been established upon inconstant variations. One stage in the life-cycle of an organism has sometimes been described as one species and another stage as a second species. Authors, failing to identify the amœbæ in their possession with the incomplete descriptions in the literature, have established new species with diagnoses as indefinite as those of their predecessors.

The determination of species of protozoa, it is true, is difficult, not only on account of the minuteness and the more or less complicated life-cycles of these unicellular organisms, but also because cultural and biologic tests, that enable the bacteriologist to determine species with a certainty second only to that of the chemist in identifying the chemical elements, have a limited application to the protozoa—how limited in their application to the parasitic amœbæ will be apparent later. Protozoölogists, therefore, are forced to rely chiefly upon morphological characters to determine species. However, I believe such characters are adequate for the purpose, if a proper discrimination be made between variable and constant characters and if all the stages in the life-cycle of an organism be taken into consideration. Many of the most obvious morphological characters of the vegetative, or trophozoite, stage of amœbæ, such as shape, size, number and shape of the pseudopods, extent of the ectoplasm and contents of the entoplasm are classically variable; on the other hand the characters of the encysted stage are relatively constant and usually absolutely diagnostic: yet the descriptions in the literature of most free-living and of many of the parasitic species are based exclusively upon the trophozoite, while the more constant and distinctive characters of the cyst have been wholly neglected. It has been my experience in studying amœbæ that, if the characters of both the trophozoite and the cyst be taken into consideration, they can always be separated into species having well-defined morphologic characteristics. Therefore, it has seemed important to undertake a careful comparative study of the amœboid organisms found microscopically and culturally in the Manila water supply, in the stools of healthy person, and in amœbic dysentery for the purpose of determining the genera and species represented, their parasitism, their cultivability on artificial media, and their relation to amœbic dysentery.

#### REVIEW OF THE LITERATURE.

*Entamœba coli* (Loesch) Schaudinn, 1903, is generally considered to be the amœba first observed by Loesch in a case of dysentery at St. Petersburg in 1875. It was carefully described by Casagrandi and Barbagallo in 1897. Schaudinn distinguished it from a pathogenic species, *Entamœba histolytica*, in 1903 and

found it in 50 per cent of the stools of healthy persons examined in East Prussia, in 20 per cent of the stools examined in Berlin, and in 66 per cent of the stools examined in the East Province. Craig (1905) found this species in 65 per cent of the stools examined from over 200 American soldiers stationed at San Francisco, California, and Vedder (1907) found it in 70 per cent of the stools of healthy natives in the Philippine Islands. *Entamœba coli*, as described by these authors, is round in the resting stage and opaque gray in color; the ectoplasm is scarcely differentiated from and is less refragent than the non-vacuolated entoplasm; the nucleus is distinctly visible in the living amœba, is situated near the center of the organism, maintains its relative position in and is not deformed by the movements of the amœba, possesses a thick nuclear membrane, and contains a relatively large amount of chromatin; its movements are sluggish and it does not ingest the red blood corpuscles of its host. This species reproduces by binary fission and by schizogony into 8 merozoites in the vegetative stage, and by sporogony which is preceded by nuclear reduction and antogamy and which results in the formation of 8 sporozoite nuclei in the encysted stage. This 8-nuclear sporocyst is the resistant stage of this amœba which serves for its transmission to a new host, in the intestine of which the 8 sporozoites are supposed to be developed. Schaudinn (1903) and Craig (1908) found *Entamœba coli* non-pathogenic for kittens. Schaudinn infected himself twice with the cysts of this species without developing dysentery.

*Entamœba histolytica* Schaudinn, 1903, was first described by Jürgens in 1902. It was distinguished from *Entamœba coli* by Schaudinn in 1903 and was found by this author in the dysenteries of Egypt, China, and Siam, and has subsequently been identified by a number of authors in the dysenteries of different countries. This species, in contrast to *Entamœba coli*, is oval in the resting amœba and transparent or greenish in color; the ectoplasm is hyaline, viscid, distinct from and more refragent than the vacuolated entoplasm; the nucleus, scarcely, if at all, visible in the living amœba, is eccentric in position, frequently changes its relative position in and is readily deformed by the movements of the amœba, possesses no limiting membrane, and is very poor in chromatin; its movements are active and it frequently ingests the red blood corpuscles of its host. *Entamœba histolytica* reproduces by binary fission, budding, and by the formation of spores which contain chromidia derived from the nucleus and which are budded off from the surface of the amœba. These spores become surrounded by a hard, impervious membrane and constitute the resistant stage that serves for the transmission of this species to a new host. Multinuclear cysts are not developed in the life-cycle of this amœba. Schaudinn (1903) and Craig (1908) found this species to be pathogenic for kittens. Craig obtained dysentery in 50 per cent of these animals by rectal injection and in 66 per cent by feeding dysenteric stools, and lesions characteristic of amœbic dysentery and containing motile *Entamœba histolytica* were found at the necropsies.

*Entamœba undulans* was observed by Castellani (1905), together with entamœbæ having the characteristics of *Entamœba histolytica*, in a case of chronic dysentery followed by abscess of the liver in a European at Colombo, Ceylon. This species is characterized by a single, long, narrow pseudopod, which is shot out from the body at short intervals and quickly withdrawn, and by an undulating membrane. No observations upon its life-cycle or pathogenicity are recorded.

*Paramœba hominis* was found by Craig (1906) in the stools of 6 natives in the Philippine Islands in which diarrhœa, associated in 3 cases with the passage of a small amount of blood, was the only symptom. This species possesses the distinct ectoplasm, the capacity for ingesting red blood corpuscles, and the active motility of *Entamœba histolytica*, but the size, nuclear structure, and encysted

stage of *Entamæba coli*; while it differs, according to Craig, from both species in its life-cycle. Besides simple division there is a development of spores within a cyst which are set free as small flagellates. The cycle is completed by the development of these flagellates into amœbæ. This organism is believed by Craig to be responsible for the diarrhœa from which the patients suffered.

*Entamæba tetragina* was first observed by Viereck (1907) in 2 cases of dysentery from India and designated by him as *Entamæba tetragina*. At nearly the same time Hartmann (1907) found this amœba in 11 cases of dysentery from Southwest Africa, and South America. He considered it to be distinct from *Entamæba histolytica* and gave to it the name *Entamæba africana*; but subsequently, becoming convinced of the identity of this amœba with that of Viereck, he withdrew the specific name *africana* in favor of the prior name, *tetragina* Viereck. Werne (1908) has also found this species in 9 cases of amœbic dysentery from Africa. More recently Whitmore (1911) has found it to be a common species in the dysenteries of the Philippine Islands and Indo-China. *Entamæba tetragina*, according to these authors, has the distinct, refrangent ectoplasm, the vacuolated entoplasm, the active motility, and the pathogenicity of *Entamæba histolytica*; but the distinct nucleus with a thick, nuclear membrane and rich in chromatin, characteristic of *Entamæba coli*. However, the nucleus of this species shows an arrangement of chromatin which, according to Hartmann, is characteristic and which serves to distinguish the vegetative stage from that of both *histolytica* and *coli*. In addition to the peripheral chromatin there is constantly present a small caryosome which exhibits cyclical changes and which in its most characteristic stage is made up of a minute centriol and a concentric ring of chromatin granules separated by an achromatic halo. This species, moreover, resembles *Entamæba coli* in its life-cycle. There is a sporogony in the encysted stage, but with the difference that 4 instead of 8 nuclei are developed in the sporo-cyst. *Entamæba tetragina* is considered to be a pathogenic species by all three authors. Hartmann found it pathogenic for kittens, but considers it less pathogenic than *Entamæba histolytica*. Sections of the intestine of experimentally infected animals showed a typical ulcerative dysentery.

*Entamæba minuta* was found by Elmassian (1909) in a case of recurrent dysentery in a European who had resided in Paraguay, South America. It possesses in the living amœba the indistinct nucleus of *Entamæba histolytica*; but the absence of a distinct ectoplasm, its sluggish movements, and its reproduction by sporogony in the encysted stage are characteristic of *Entamæba coli*; and it is distinguished from both these species by its small size, averaging from 12 to 14 microns in diameter, and by the development of 4 instead of 8 nuclei in the sporocyst. In this latter particular it corresponds with *Entamæba tetragina* Viereck. Elmassian believes that both *Entamæba minuta* and *Entamæba coli* may, under certain conditions, become pathogenic.

*Entamæba nipponica* was observed by Koidzumi (1909) in Japan, at first together with *Entamæba histolytica* in advanced cases, later in early cases of amœbic dysentery, and also in dysentery of bacillary origin. This species corresponds with *Entamæba histolytica* in possessing a well differentiated ectoplasm, a vacuolated entoplasm, a thin nuclear membrane, and the capacity for ingesting red blood corpuscles, but with *Entamæba coli* in the richness of its nucleus in chromatin and in reproduction by schizogony in the vegetative stage; but it differs from all other species hitherto described in the arrangement of the chromatin in the forms of 3 to 8 discrete clumps on the inner surface of the nuclear membrane. Sporogony in the encysted stage was not observed. This species is considered non-pathogenic by Koidzumi.

Akashi (1911) has recently described 4 species of amœbæ parasitic in the intestinal tract of man in Japan. Two of these are considered by this author as probably identical with *Entamœba coli* and *Entamœba histolytica* respectively; one he designates as *Entamœba tetragina*, but states that he does not consider it identical with the *tetragina* species of Viereck; and the fourth is said to be a new species which the author does not designate by name. The descriptions of these species are in Japanese with a brief abstract in German. The chief point of interest in the inadequate descriptions (in German) is that reproduction takes place by "schizogony" in the encysted stage in the two latter species, with the formation of 4 nuclei in "*Entamœba tetragina*" and the number of nuclei not stated in *Entamœba* sp.

Musgrave and Clegg (1904) succeeded in producing a disease in monkeys and man having the symptoms and lesions characteristic of amœbic dysentery, by introducing into the intestinal tract of the experimental animals cultures of amœbæ grown in symbiosis with pure cultures of bacteria on an alkaline agar medium consisting of beef extract 0.3 to 0.5, sodium chloride 0.3 to 0.5, agar-agar 20.0, distilled water 1000.0, and made 1 per cent alkaline to phenolphthaleïn, not only from cases of amœbic dysentery but also from lettuce and from the Manila water supply; and they were able, in certain cases at least, to recover in cultures amœbæ from the experimentally infected animals. These authors, therefore, concluded that any amœba may become pathogenic when introduced into the intestinal tract of man.

Lesage (1905) cultivated an amœba in 7 out of 30 cases of amœbic dysentery on a culture medium consisting of agar which had been washed for a week in large quantities of distilled water and on which the growth of bacteria was largely inhibited. This amœba presented many of the characters of Schaudinn's pathogenic *Entamœba histolytica* and is believed by this author to be the pathogenic species. Lesage in a subsequent paper (1907) states that leucocytic extract is a particularly suitable medium for the cultivation of the pathogenic amœbæ. This medium is prepared from the leucocytic exudate of the guinea pig. The exudate is kept on ice for 24 hours and then centrifugated. The clear, supernatant fluid is employed as the culture medium. In this medium Lesage cultivated amœbæ from cases of amœbic dysentery which were pathogenic. In 1908 Lesage cultivated a non-pathogenic amœba from the intestinal tract of man in the Tropics, which is said to represent several varieties, and which this author considers to be the non-pathogenic species of tropical countries, distinct from the non-pathogenic *Entamœba coli* of temperate climates, and to which he gave the name, *Entamœba tropicalis*.

Walker (1908) cultivated amœbæ in symbiosis with bacteria on Musgrave and Clegg's medium, from the intestinal tracts of a large number of animals. These amœbæ included one species designated as *Amœba hominis* from man. These cultures were made post-mortem from the intestines of the animals and were consequently believed to be true parasites.

Gauduchau (1908) cultivated an amœba, *Entamœba phagocytoides*, from a case of amœbic dysentery in Hanoi, Indo China, on ordinary agar, potato, and other media inoculated with *Bacillus typhosus* or other bacilli. This amœba ingests red blood corpuscles, multiplies by binary and multiple fission, and produces spirilla-like bodies in its cytoplasm.

Noc (1909) was able to cultivate an amœba three times from amœbic liver-abscesses and in five out of seven attempts from dysenteric stools in Indo China on an agar culture medium 0.5 per cent alkaline to phenolphthaleïn. The same species was also cultivated from the water. This amœba differs in its morphology

and life-cycle from *Entamoeba coli*, *Entamoeba histolytica*, and *Entamoeba tetragina*. Noc believes this amoeba to be the cause of the amoebic dysentery and liver abscesses of that country. The cysts of this amoeba, he says, are especially abundant in the surface waters of Indo China during the rainy season which corresponds with the exacerbation of endemic dysentery. However, he was unable to produce dysentery in kittens or monkeys with his cultures from water or dysenteric stools.

Werner (1908) was unable to obtain vegetative forms of either *Entamoeba histolytica* or *Entamoeba tetragina*, but did secure growth and cyst formation of *Amoeba limax*, a common water amoeba, in his cultures from dysenteric stools on Musgrave and Clegg's medium. Therefore, he is of the opinion that the amoebæ cultivated by Musgrave and Clegg (1904), Walker (1908), and others from the intestinal tract of man and other animals are cysts of similar free-living amoebæ which have been ingested with water or food, have passed unchanged through the intestine, and have found conditions favorable for development when the faeces have been placed on the culture medium.

Whitmore (1911) has also come to the conclusion that the amoebæ cultivated by him at Manila from dysenteric stools are free-living amoebæ of the *limax* type and not parasitic amoebæ.

#### AMOEBAE IN THE MANILA WATER SUPPLY.

In consideration of the somewhat general belief in the Orient that the amoebæ in the water are the source of infection in amoebic dysentery, and in consequence of the cultural and experimental work of Noc (1909) Williams and Gurley (1909), and especially of Musgrave and Clegg (1904), who state that they have produced dysentery in monkeys and man with amoebæ cultivated from the Manila water supply, it has seemed desirable that a study be made of these for comparison with those found in the intestinal tract of man.

The Manila water supply comes from an uninhabited watershed of the Mariquina River and its tributaries. The water is stored in a reservoir on the watershed by a dam constructed across a narrow gorge in the Mariquina Valley at Montalban about 24 kilometers from Manila. It is conducted from this reservoir in closed water-mains to Manila, where it is distributed in branch mains and pipes to the various taps in the city. The water, therefore, is presumably free from faecal contamination and should contain only the normal amoebic fauna of that watershed.

Samples of this water have been collected at different times from different taps in Manila for examination. In each case about 200 cubic centimeters of the water have been drawn directly from the tap into a sterile Erlenmeyer flask and about 2 cubic centimeters of ordinary nutrient bouillon added to enrich it and favor the multiplication of organisms present in the sample. The flasks, plugged with sterile cotton, were kept at room temperature and the contents examined from day to day for amoebæ. In two or three days a scum forms on the surface of the water which, if examined microscopically, will be found to consist of bacterial and protozoan growth, among the latter amoebæ are usually present. If a loop-full of this material containing amoebæ be transplanted to the surface of solidified Musgrave and Clegg's medium in a Petri dish an abundant growth of amoebæ will be obtained in a few days.

Twenty-five samples of tap water from the Manila supply have been examined microscopically, after enriching and incubating at room temperature, and by cultures made on Musgrave and Clegg's medium. As the study of the parasitic amœbæ progressed it became apparent that it was unnecessary to examine a larger number of samples, to concentrate the amœbic fauna by filtration of large quantities of the water, or to study the amœbæ from other surface waters, as had been originally intended. In 23 out of the 25 samples of water amœbæ were found microscopically and culturally. In addition to these 23 cultures of amœbæ, one culture isolated by Dr. A. W. Sellards in the Biological Laboratory of the Bureau of Science, and one isolated by Dr. E. B. Vedder at the Division Hospital of the United States Army from the Manila water supply have been studied.

Of these 25 cultures of amœbæ, twenty-four have been found to be of one and the same species (Plate I, figs. 1 and 2); one culture was a distinct species (Plate I, fig. 3). Both species appear to belong to the so-called *limax* group of water amœbæ, but because of the imperfect descriptions I have not attempted to identify them with the names in the literature, or to add to the confusion by giving them new names; nor is it necessary; it is sufficient for our purpose to determine the generic characters of these two species. This type of amœboid organism (figs. 1 to 3) is characterized by an amœboid trophozoite in which the nucleus is situated centrally in the resting organism and in which the chromatin of the nucleus is collected into a relatively large and dense karyosome that is surrounded by an achromatic halo, which possesses with rare exceptions, a contractile vacuole, and which reproduces by binary fission and by spore-formation (Walker, 1908); by an encysted stage that has a single nucleus of the same structure as that of the trophozoite, and in which no reproduction takes place; and by multiplying and encysting freely upon artificial culture media. These characters are those of the genus *Amœba* Erenberg of which *Amœba protens* Leidy is the type species.

#### AMŒBÆ CULTIVABLE FROM THE INTESTINAL TRACT OF MAN.

The material from which these cultures have been made has consisted of fresh stools containing amœbæ from 113 healthy persons or persons suffering from diseases other than amœbic dysentery, and from 21 cases of amœbic dysentery, and pus containing amœbæ from 2 cases of amœbic liver-abscess, obtained from the drainage tube after operation and, also, in one of the cases, post-mortem from the infected liver. This material has been obtained chiefly from the hospital of Bilibid Prison, but in part from the different hospitals in Manila. I am indebted to the physicians in charge of these hospitals and to several of my colleagues

in the Bureau of Science for the opportunity and for the assistance in obtaining it.

The culture medium employed has been for the most part the standard medium of Musgrave and Clegg (1904). Several modifications of this medium have been tried, including the substitution of nutrient bouillon, peptone, dextrose, or peptone and dextrose for the beef extract, and leaving out the salt and nutrient substances altogether. The cultivable amœbæ appear to grow equally well on any of these media. The methods employed in making these cultures and in isolating pure cultures of the amœbæ are those devised by Musgrave and Clegg (1904) and by me (Walker 1908) and are sufficiently well known not to need repetition here. It has not been considered necessary in this morphologic study to isolate the pure cultures of amœbæ with pure cultures of bacteria.

Two hundred and seventy-nine cultures have been made from the stools of 113 cases of amœbiasis without symptoms of dysentery, 158 cultures from the stools in 21 cases of amœbic dysentery, and 27 cultures from the pus of 2 cases of amœbic liver-abscess, in all 464 cultures from 136 cases of amœbiasis. These cultures have been made in every case from fresh material in which living amœbæ had been demonstrated microscopically, usually in the motile condition, sometimes encysted, and often in large numbers.

Growth of amœbæ in the cultures was obtained in 6, or 5.3 per cent, of non-dysenteric cases, and in 2, or 9.2 per cent, of the cases of amœbic dysentery. All of the 27 cultures from the 2 cases of amœbic liver-abscess were negative. Growth of mastigamœbæ, flagellates, and ciliates was obtained in the cultures from several of the cases. In addition to these 8 cultures of amœba grown by myself from the intestinal tract of man, one culture isolated by Dr. E. B. Vedder from a non-dysenteric stool at the Division Hospital in Manila, one culture isolated by Dr. Marshall A. Barber from a case of diarrhœa in Kansas, one stock culture in the Biological Laboratory of the Bureau of Science from a case of amœbic dysentery, and one culture isolated by Musgrave and Clegg (1904) from a case of amœbic dysentery in Manila have been available for study.

A study of these 12 cultures has disclosed 5 well defined species (Plates II and III). Among the 8 cultures from persons showing no symptoms of dysentery there are 4 different species. Among the 4 cultures from cases of amœbic dysentery as many different species are represented. Of the latter, amœba 8 is the same species as amœbæ 1 and 20,850 from non-dysenteric stools (Plate II, fig. 4); amœba 14,965 is the same species as amœbæ 7, 7,658, and 20,998 from non-dysenteric stools (Plate II, fig. 5); and amœba 7,671 is the same species as the amœba isolated by Barber from a case of diarrhœa in Kansas (Plate II, fig. 6 and Plate III, fig. 7). Amœba 9 grown from a non-dysenteric stool and amœba "L" isolated by Musgrave and Clegg (1904) from a dysenteric stool (Plate III, fig. 8) are not duplicated among the cultures. However, amœba 9 is of the same species as the amœba cultivated from 22 out of 25 samples of water



from the Manila water supply (Plate I, figs. 1 and 2). For reasons already stated no attempt has been made to identify these species with species named in the literature; it is sufficient for our present purpose, as in the case of the water amœbæ, to determine the genus to which they belong. All 5 species cultivated from both non-dysenteric and dysenteric stools possess the characters of the genus *Amœba* Ehrenberg described in the previous section (Compare figs. 1 to 3 with figs. 4 to 10).

#### AMŒBÆ FOUND MICROSCOPICALLY IN THE INTESTINAL TRACT OF MAN.

This part of the investigation has included a microscopic study of the living amœbæ in the fresh stools from 142 cases of amœbiasis without symptoms of dysentery, from 28 cases of amœbic dysentery, and in the pus of 2 cases of amœbic liver-abscess; of fixed and stained preparations from 21 cases of amœbiasis without symptoms of dysentery and from 16 cases of amœbic dysentery; and in sections of the intestine in 1 case of amœbic dysentery, and of the liver in 2 cases of amœbic liver-abscess. I am indebted to Dr. E. R. Stitt of the United States Naval Hospital, Cañacao, Cavite, for a section of one of the cases of amœbic liver-abscess and to Dr. V. L. Andrews of the College of Medicine and Surgery, University of the Philippines, for sections of the other case of amœbic liver-abscess and sections of the intestine from a case of amœbic dysentery.

The stools have been studied fresh in ordinary cover-glass and slide preparations. Stained preparations of the fæces and of the pus from liver abscesses have been made by spreading thin smears on cover-glasses, floating them "wet" on the surface of Zenker's fluid for 5 minutes, washing in water until the fixing fluid is removed, staining 5 minutes in aqueous alum hæmatoxylin, washing in distilled water, dehydrating in different grades of alcohol, clearing in oil origanum, and mounting in xylol balsam. I have found Zenker's fluid preferable to Schaudinn's alcohol-corrosive-sublimate mixture as a fixative for amœbæ. Aqueous alum hæmatoxylin has proved a more precise stain for the chromatin of amœbæ than iron hæmatoxylin or any other stain that I have tried. The sections from one case of amœbic liver-abscess were stained with iron hæmatoxylin, and from the other case of liver abscess and from the dysenteric intestine with hæmatoxylin and eosin.

One type of amœboid organism has been found exclusively in all of this material (Plate IV, figs. 9 to 12 and Plate V, figs. 13 to 16). This differs from the *Amœba* type found in the Manila water supply and cultivable from the intestinal tract of man in certain fundamental morphological and biological characters. The trophozoite has the nucleus situated excentrically instead of centrally in the resting organism; the chromatin is arranged peripherally instead of centrally in the nucleus; there is no contractile vacuole; reproduction by sporulation does not occur; and multiplication does not take place on ordinary artificial media. The cyst contains 4 or 8 nuclei instead of a single nucleus; a reproductive process takes place in the cyst; and encystment occurs only in the body

of the host (Compare figs. 1 to 8 with figs. 9 to 16). I believe, the characters of this type of amœboid organism are sufficiently distinct from the *Amœba* type to justify the establishment of the new genus, *Entamœba*, by Casagrande and Barbagallo (1897) and its adoption by Schaudinn (1903). This genus should include the parasitic amœbæ of man and also the parasitic amœbæ that have been described in certain lower animals, namely: *Entamœba ranarum* (Grassi) Dobell, 1908, in the frog, *Entamœba testudinis* Hartmann, 1910, in the turtle, *Entamœba muris* (Grassi, 1881) Wenyon, 1907, in the mouse, and *Entamœba nutalli* Castellani, 1908, in the monkey.

What, then, is the significance of the species of the genus *Amœba* cultivable from the intestinal tract of man and other animals?

These cultivable amœbæ might be considered parasitic entamœbæ that had undergone modification by their growth on artificial culture media. It seems possible that such a change in environment might modify some of the less constant morphologic characters of these organisms, such as size, shape, number of pseudopods, extent of the ectoplasm, and granulation or vacuolization of the entoplasm; but that it could cause a complete reorganization of the structure of the nucleus, develop *de novo* such a constant organelle as a contractile vacuole, or profoundly modify the life-cycle of the organism appears doubtful. Moreover, that the supposed modification resulting from cultivation on artificial media should invariably take the form of a change from the characters of the genus *Entamœba* to those of the genus *Amœba* is, to say the least, improbable.

It might be claimed that, owing to some fault in my technique, I had failed to cultivate the parasitic entamœbæ. Among my cultures are four isolated by as many different investigators, other than myself, two of which are from cases of amœbic dysentery and one of these isolated by Musgrave and Clegg (1904); all of these cultures, like my own, are of the *Amœba* type. Werner (1908) failed to cultivate entamœbæ from cases of amœbic dysentery. Dobell (1908) and Weryon (1907) also were unable to cultivate on artificial media the entamœbæ which they found in the intestines of lower animals. An examination of the descriptions and illustrations of amœboid organisms cultivated by different authors shows in every case organisms not of the *Entamœba* but of the *Amœba* type.

There still remains the possibility that the cultivable amœbæ, as well as the non-cultivable entamœbæ, are parasitic in the intestinal tract of man. Since, however, organisms of the *Amœba* type are not found in the microscopic examination of fresh or stained preparations of fæces, liver-abscess pus, or in sections of liver or intestine, it seems probably that the amœboid organisms cultivated by Musgrave and Clegg (1904), Lesage (1905, 1908), Gauduchea (1908), and Noc (1909) from the intestine and liver abscesses of man, and by myself (Walker 1908) from

the intestine of man and other animals, are at most only temporary commensals in the intestinal tract, and more probably that they are, as Werner (1908) has suggested, only cysts of free-living amœbæ which have been ingested with water or food and have passed unchanged through the intestinal canal.

The entamœbæ found in the stools of healthy persons or of persons suffering from disease other than dysentery present characters that correspond in part with those of *Entamœba coli* Schaudinn and in part with those of *Entamœba nipponica* Koidzumi. In stools of such persons, in which there exists a natural diarrhœa or diarrhœa induced by a cathartic, the vegetative or trophozoite forms are commonly present. The living trophozoite is rounded in the resting condition, 7.5 to 34.5  $\mu$  in diameter, oval, ligulate or irregular when in motion, and porcelainous and refragent in appearance. The ectoplasm is ordinarily visible only in the pseudopods. There is no contractile vacuole and the entoplasm is normally free from all vacuolization. The nucleus is distinctly visible in the living entamœba. It occupies an eccentric position, but in the rotation of the rounded entamœba the nucleus frequently appears central in optical section. It has the form of a rather heavy ring of refragent material, that may be of uniform or of irregular thickness, which surrounds a non-refractive nucleoplasm and within which there may or may not be present a few refractive granules. The movements of these entamœbæ are sluggish, even in fresh stools and they quickly lose all motility in cold stools.

In preparations fixed wet and stained with aqueous alum hematoxylin the trophozoite shows a deeply-staining granular cytoplasm, usually without distinction from the ectoplasm. Occasionally a narrow rim of homogeneous, more feebly-staining ectoplasm is present. The ringform nucleus is seen in optical section to consist of a nuclear membrane enclosing an achromatic nucleoplasm and a relatively large amount of chromatin. Two varieties in the distribution of the chromatin in the nucleus can be distinguished. In the first of these the chromatin appears in optical section as a continuous, segmented or granular ring of approximately uniform thickness about the inner surface of the nuclear membrane, with or without some granular chromatin scattered in the nucleoplasmic network or collected in a small karyosome. This variety corresponds with the *coli* species of Schaudinn (fig. 9). In the second variety the chromatin is collected in several discrete clumps on the inner surface of the nuclear membrane. This variety corresponds with the *nipponica* species of Koidzumi (fig. 10).

Reproduction in the trophozoite appears to take place exclusively by simple division. I have seen no evidence of a schizogony, such as described by Schaudinn in *Entamœba coli* and by Koidzumi in *Entamœba nipponica*, in either fresh or stained preparations.

In non-dysenteric stools that have become formed encysted entamœbæ make their appearance. These cysts (fig. 11) are developed, as in the case of the order Coccidiida, only in the intestinal tract of the host, and not in the evacuated fæces. If the process of encystment has already begun before the entamœbæ are passed in the stool the development of the cysts may continue outside of the host; but motile and resting entamœbæ quickly degenerate and disintegrate in cold stools. The mature cysts usually contain 8 nuclei of the same structure, but smaller and poorer in chromatin than the nuclei of the trophozoite; cysts containing more than 8 nuclei are occasionally seen. Whether such cysts represent a different species or variations in the same species, it is difficult to say. In the development of these cysts Schaudinn described a complicated series of nuclear changes, including an autogamous copulation of reduced nuclei, that preceded the formation of the 8 nuclei in the mature cyst. Such a reproductive process would constitute a sporogony comparable with that taking place in the order Coccidiida. The mature cyst would correspond with the sporocyst and the nuclei to the nuclei of the 8 sporozoites that are supposed to be developed when the cyst reaches the intestine of a new host. However, I have been unable to observe any stages in the development of the 8 nuclei in the cysts which could be interpreted otherwise than straight-forward nuclear division. Dobell (1909) has come to the same conclusion from his study of the development of the multinuclear cysts of *Entamœba ranarum*. If this interpretation of the process be correct then it must be considered either as a schizogony in which the cyst would be a schizocyst and the 8 nuclei the nuclei of the merozoites that are developed in the intestine of the new host; or possibly as a gametogony, comparable to that occurring in the order Gregarinida, in which the 8 nuclei would constitute the nuclei of gametes that are formed and which copulate in the intestine of the new host.

Entamœbæ of the *coli* and *nipponica* varieties have been observed only in the stools of healthy persons or of persons suffering from diseases other than dysentery; but it is possible that they might occasionally be found associated with another type of entamœba, about to be described, in dysenteric stools. In such cases they would represent double infections. Of the two varieties the *coli* is found much the more frequently. The *nipponica* variety may be encountered alone, alternating with the *coli* variety in different stools of the same patient, or associated with the *coli* variety in the same stool. Transitional forms between the two varieties are frequently seen, and the 8-nuclear cysts have been found associated with both the *coli* and the *nipponica* varieties of entamœba.

The entamœbæ found in the stools of cases of amœbic dysentery, in the pus of amœbic liver-abscesses, and in sections of dysenteric intestines and of amœbic liver-abscesses, present certain morphological differences from the entamœbæ found in non-dysenteric stools which appear to be

fairly constant, and which in their sum serve to distinguish the entamœbæ from the two sources. The characters of the entamœbæ from dysenteric material correspond in part with those of *Entamœba histolytica* Schaudinn, in part with those of *Entamœba tetragina* Viereck and, under certain conditions, with those of *Entamœba minuta* Elmassian. The trophozoites in fresh stools in acute dysentery are usually, but not invariably, larger, more often oval in the resting condition, and more hyaline and less refrangent in appearance than the trophozoites from normal stools. The cytoplasm is uniformly hyaline in appearance with no distinction between ectoplasm and entoplasm. It contains a variable amount of granular material and often red blood corpuscles of the host as inclusions which, when collected near the center of the organism, leave a hyaline periphery that has the appearance of an extensive ectoplasm described by other authors. There is no contractile vacuole and the entoplasm is normally free from other vacuoles; it is only following changes in temperature or tonicity of the medium or in consequence of degenerative changes that vacuolization is present. The position of the nucleus is eccentric, and in the more actively motile entamœbæ in dysenteric stools the nucleus more frequently changes its relative position and is more subject to pressure that tends to deform it than the nucleus of the more sluggish entamœba in normal stools. The nucleus, in contrast to entamœbæ of the *coli* and *nipponica* varieties, is usually distinguished with difficulty in the living trophozoite. Contrary to Schaudinn I distinguish a thin but distinct nuclear membrane. This membrane encloses a homogeneous nucleoplasm which is slightly less refrangent than the surrounding cytoplasm and which contains a small amount of granular material arranged about the inner surface of the nuclear membrane and scattered in the nucleoplasm. In consequence of this thin peripheral layer and the low index of refraction of the nucleoplasm the nucleus has the appearance of an extremely pale vacuole and is distinguished with difficulty, especially in motile or vacuolated entamœbæ. These entamœbæ, in contrast to those of normal stools, exhibit an active motility in fresh stools which often persists in cold stools several hours old.

In preparations that have been fixed wet in Zenker's fluid and stained with aqueous alum hematoxylin the trophozoite in dysenteric stools usually stains feebly and shows a reticulated rather than a granular structure of the cytoplasm with no distinction between ectoplasm and entoplasm. In the stained preparations the difference in the appearance of the nucleus from the nucleus of entamœbæ in non-dysenteric stools is seen to be due to the much smaller amount of chromatin in the nucleus of the dysenteric entamœbæ. Two varieties in the distribution of the chromatin can be distinguished. In the one the chromatin is extremely scanty and is arranged as a barely perceptible layer about the inner surface of the

nuclear membrane, with or without a minute karyosome or a few scattered fragments in the nuclear-network. This variety corresponds with the *histolytica* species of Schaudinn (fig. 12). In the second variety the chromatin is rather more abundant and is arranged in part as a loose granular layer, that frequently shows radial projections, about the inner surface of the nuclear membrane, and in part as a loose central karyosome which, in its most typical form, consists of a minute centriol surrounded by an achromatic halo that is bounded by a circle of chromatin granules. This variety corresponds with the *tetragina* species of Viereck and Hartmann (fig. 13).

During the active phase of amœbic dysentery only the trophozoites of these entamœbæ are present in the stools. With aqueous alum hematoxylin, which is an extremely precise stain for the chromatin of entamœbæ, only stages of binary fission have been observed. I have been unable to find any of the chromidial stages that are said by Schaudinn, Craig and Hartmann to precede the formation of spores in *Entamœba histolytica*. It seems possible that the use of iron hematoxylin or other less precise chromatin stains may have resulted in mistaking bacteria or protoplasmic granules for chromatin. I have not observed any of the later stages of the formation of the spores or the free spores in either fresh or stained preparations.

When the acute symptoms in untreated dysentery have passed and the stools of the patient are becoming normal the trophozoites become smaller, less actively motile and more rounded in the resting forms, and the chromatin becomes more abundant in the nucleus. These changes are preparatory to the development of the cysts. Such forms resemble the *minuta* species of Elmassian (fig. 14). Finally, encysted forms containing 4 nuclei appear which may persist for an indefinite period or until the patient suffers an exacerbation of the acute symptoms. Thus in amœbic dysentery 6,442 there appeared in the stools on January 30, 1911, a considerable amount of mucus and pus streaked with blood. On January 31 the stools were partly formed and partly fluid, consisting of mucus, pus, and blood and containing many amœboids, resting and encysting entamœbæ. The amœboid and resting entamœbæ were small but with the *histolytica* type of nucleus, the encysted forms were the cysts of the *tetragina* type containing 4 nuclei. The symptoms abated without treatment, the stools became normal, and the patient has had no recurrence of the disease; but the cysts containing 4 nuclei have persisted in the stools up to the present time (August 23, 1911). Still more instructive is the following chronic case, amœbic dysentery 5,748, which came down with a typical attack of amœbic dysentery on April 29, 1911, with mucus, pus, and bloody stools containing many large entamœbæ of the *histolytica* type (fig. 12). The patient was put under treatment to which he promptly responded, the symptoms abated and the stools became normal.

Cysts of the *tetragina* type then appeared in the stools. On June 1 the patient suffered a relapse with some mucus, pus, and blood in the stools and typical *Entamæba histolytica* were present in the stools. This condition has persisted intermittently in spite of treatment with ipecac until August 1 when the stools became free from mucus and blood. On August 7 they had become formed and the 4-nuclear cysts again appeared in the fæces.

The cysts containing 4 nuclei found in the stools of cases of amœbic dysentery, like the cysts containing 8 nuclei in non-dysenteric stools, are developed only in the intestinal tract of the host and not in the defecated stools. They differ from the 8-nuclear cysts in non-dysenteric stools, not alone in the different number of nuclei contained in the mature cysts, but, also, in a number of other particulars. The cysts are smaller; the nuclei are larger and contain more chromatin; the multiplication of the nuclei appears to take place earlier in the encystment of the entamœba, often even in the amœboid stage; the cyst wall, although equally impermeous to stains, appears not to be so thick or well defined; and the encysting entamœba more frequently contains elongated refrangent bodies which stain deeply with iron hematoxylin, but which do not stain with the more precise aqueous alum hematoxylin, and which, therefore, are probably protoplasmic or foreign bodies rather than chromatin. (Compare fig. 11 with fig. 16.) In the development of these cysts, as in the development of the cysts from non-dysenteric stools, no indication of nuclear reduction and autogamy such as is described by Hartmann in the development of the cysts of *Entamæba tetragina*, have been observed, but only uncomplicated nuclear division (figs. 14 to 16). If these observations be correct then these cysts, like the cysts of *Entamæba coli*, would have to be considered either schizogenic or possibly gametogenic rather than sporogenic.

Entamœbæ of the *histolytica* and the *tetragina* varieties have been found only in the stools or tissues of persons suffering from or having a history of amœbic dysentery. The *histolytica* type I find, contrary to Whitmore (1911), to be the more common variety in the dysenteries of Manila. The *tetragina* variety when found, invariably has been associated with the *histolytica* and transitional forms between the two varieties are common. Moreover the *tetragina* cysts, as the protocols of the above cited cases show, have been found associated with pure *histolytica* infections.

In view of the observations that have been presented in detail in the preceding pages I am of the opinion that, although several of the varieties of entamœba hitherto described are represented, only two well defined species are found parasitic in the intestinal tract of man. One of these species includes the *coli* variety of Schaudinn and the *nipponica* variety of Koidzumi. This species is characterized by its porcelaneous and

refrangent appearance, distinct nucleus and sluggish motility, in the living *Entamæba coli*; by the deeply staining, granular cytoplasm, and by the relatively large amount of chromatin, which is arranged either as a heavy continuous or broken ring (*coli* variety) or as several discrete masses (*nipponica* variety) on the inner surface of the nuclear membrane, with transitions between these two varieties, in the stained *Entamæba coli*; and especially by the development of cysts containing 8 nuclei. This species should, according to the law of priority, bear the name of *Entamæba coli* Schaudinn. It is found in the stools of healthy persons and of persons suffering from diseases other than dysentery and is, therefore, presumably non-pathogenic. The other species include the *histolytica* variety of Schaudinn, the *tetragina* variety of Viereck and Hartmann and probably the *minuta* variety of Elmassian. It is characterized by its hyaline and feebly refrangent appearance, indistinct nucleus, and active motility in the living *Entamæba coli*; by the feebly-staining reticulated cytoplasm, and by the relative paucity of chromatin which is arranged either as a barely perceptible layer about the inner surface of the nuclear membrane with or without a few fragments scattered in the nuclear network (*histolytica* variety), or as a more extensive but loose, granular peripheral layer and a loose central karyosome (*tetragina* variety), with transitions between these two varieties in the stained *Entamæba coli*; and especially by the development of cysts containing 4 nuclei. This species is found only in the stools, pus, or tissues of cases of amœbic dysentery, amœbic liver-abscesses, or of cases having a history of amœbic dysentery and is probably a pathogenic species. According to the law of priority this species should bear the name, *Entamæba histolytica* Schaudinn. The differences in the arrangement of the chromatin in the nuclei of the *coli* and *nipponica* varieties and of the *histolytica* and *tetragina* varieties probably represent metabolic or reproductive changes in the nuclei of the two species. This view is supported by the presence of forms showing a chromatin arrangement intermediate between these varieties of the two species. It is probably that other imperfectly described species of *Entamæba* that have been observed in the intestine of man would be found, on a more complete knowledge of their morphology and life-cycles, to belong to one or the other of these two species.

The most important practical application of these differences in morphology between *Entamæba coli* and *Entamæba histolytica* is the microscopic diagnosis of amœbic dysentery, especially in incipient or chronic cases, as a guide to treatment and prophylaxis.<sup>1</sup> The differentiation of

<sup>1</sup>It is to be noted in this connection that the microscopic diagnosis of amœbic dysentery is not dependent upon *Entamæba histolytica* being the primary etiologic factor in this disease, but only upon the apparently constant association of this *Entamæba* with amœbic dysentery.



*Entamæba histolytica* from *Entamæba coli* must frequently be made without the help of the characteristic encysted stages. While the diagnosis in the trophozoite stage is not easy, it can be made with certainty by a protozoölogist having sufficient experience and using proper care. The examinations for this purpose should be made of perfectly fresh stools, repeated if necessary on different days, and should be made, if any uncertainty exists, of stained as well as of fresh preparations. Preparations fixed wet in Zenker's fluid and stained with aqueous alum hematoxylin should be employed for this purpose. Greater difficulty may be experienced in diagnosing chronic cases between the periods of exacerbation of the acute symptoms, in which *Entamæba histolytica*, in preparation for encystment more closely resembles in some respects *Entamæba coli*; but under these conditions a careful search will usually disclose the presence of 4-nuclear cysts. The presence of such cysts in the stool is absolutely diagnostic of *Entamæba histolytica*; but a diagnosis from the presence of 8-nuclear cysts in the stool must be made with caution, since there might exist a double infection with *Entamæba coli* and *Entamæba histolytica*.

An experimental study of the parasitism and pathogenicity of the species of the genera *Amæba* and *Entamæba*, established by this morphologic study, has been undertaken and the results of it will be presented in another paper.

#### SUMMARY AND CONCLUSIONS.

1. The amœboid organisms found in the Manila water supply belong to the genus *Amæba* Ehrenberg.
2. The amœboid organisms cultivable from the intestinal tract of man, both from healthy persons and from cases of amœbic dysentery, also belong to the genus *Amæba* Ehrenberg.
3. The cultivable species of the genus *Amæba* are not parasitic in the intestinal tract of man; when obtained in cultures from the intestine they probably are derived from cysts of amœbæ that have been ingested with water or food and have passed unchanged through the intestinal tract.
4. The amœboid organisms parasitic in the intestinal tract of man belong to a distinct genus, *Entamæba* Casagrandi and Barbagallo.
5. The entamœbæ are strict or obligatory parasites and are incapable of multiplication outside of the body of their host. They can not be cultivated on Musgrave and Clegg's medium.
6. One non-pathogenic species of the genus *Entamæba*, *Entamæba coli* Schaudinn, parasitic in the intestinal tract of man, which includes *Entamæba nipponica* Koidzumi, and which develops cysts containing 8 nuclei, is recognized.
7. One presumably pathogenic species of the genus *Entamæba*, *En-*

*Entamoeba histolytica* Schaudinn, which includes *Entamoeba tetragina* Viereck, and which develops cysts containing 4 nuclei, is recognized.

8. A differential diagnosis of an infection with *Entamoeba coli* from an infection with *Entamoeba histolytica* can be made with the microscope.

9. An infection with either *Entamoeba coli* or *Entamoeba histolytica* must always come directly or indirectly from another infected person.

10. Water or uncooked food can transmit amœbic dysentery only when contaminated with faecal matter from a case of amœbic dysentery.

11. The infection with *Entamoeba histolytica* may persist for an indefinite period after the symptoms of amœbic dysentery have disappeared, during which time the resistant, encysted entamoebæ may be passed in large numbers in the stools and constitute an important source of infection to others. Such persons are "carriers" of amœbic dysentery, comparable to the "carriers" of typhoid fever or cholera.

12. The prophylactic measures for the prevention of amœbic dysentery are sufficiently indicated by the preceding conclusions; they are identical with those required for the prevention of other specific infectious diseases of the intestinal tract, like typhoid fever and cholera.

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## ILLUSTRATIONS.

(From photomicrographs by Charles Martin.)

### PLATE I.

- FIG. 1. *Amœba* 1, trophozoite, culture from the Manila water supply.  $\times 1000$ .  
2. *Amœba* 1, cysts, culture from the Manila water supply.  $\times 1000$ .  
3. *Amœba* 19, trophozoite and cyst, culture from the Manila water supply.  $\times 1000$ .

### PLATE II.

- FIG. 4. *Amœba* 8, trophozoite and cysts, culture from a stool of a case of amœbic dysentery.  $\times 1000$ .  
5. *Amœba* 14,965, trophozoites, culture from a stool of a case of amœbic dysentery.  $\times 1000$ .  
6. *Amœbæ* 7,671, trophozoite, culture from a stool of a case of amœbic dysentery.  $\times 1000$ .

### PLATE III.

- FIG. 7. *Amœba* 7,671, cysts, culture from a stool of a case of amœbic dysentery.  $\times 1000$ .  
8. *Amœbæ* "L" (Musgrave and Clegg), trophozoite, culture from a stool of a case of amœbic dysentery.  $\times 1000$ . This species differs from *Amœba* 7,671 (figs. 6 and 7) chiefly in not possessing a contractile vacuole.

### PLATE IV.

- FIG. 9. *Entamœba coli*, trophozoite, in the stool of a healthy person.  $\times 1000$ .  
10. *Entamœba coli* var. *niponica*, trophozoite, in the stool of a healthy person.  $\times 1000$ .  
11. *Entamœba coli*, cyst containing 8 nuclei only 5 of which are shown in the optical section of the entamœba, in the stool of a healthy person.  $\times 1000$ .  
12. *Entamœba histolytica*, trophozoite containing red blood corpuscles, in the bloody and mucus stool of a case of amœbic dysentery (No. 5,748).  $\times 1000$ .

### PLATE V.

- FIG. 13. *Entamœba histolytica* var. *tetragina*, trophozoite containing red blood corpuscles, in the stool of a case of acute amœbic dysentery.  $\times 1000$ .  
14. *Entamœba histolytica*, trophozoite in preparation for encystment, in the stool of a case of chronic amœbic dysentery.  $\times 1000$ .  
15. *Entamœba histolytica*, encysting entamœba showing the first division of the nucleus, in the stool of a chronic case of amœbic dysentery.  $\times 1000$ .  
16. *Entamœba histolytica*, cyst containing 4 nuclei, in the stool of a chronic case of amœbic dysentery.  $\times 1000$ .



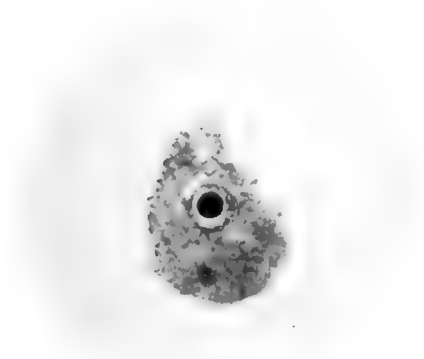


FIG. 1.

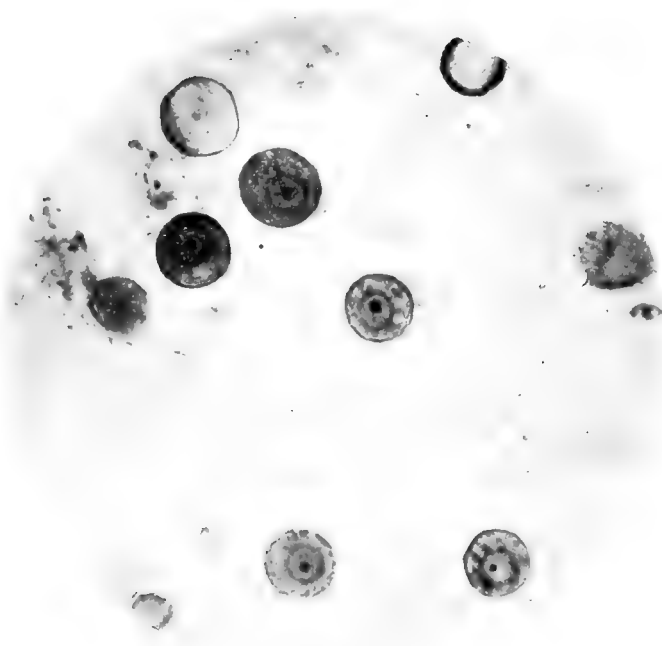


FIG. 2.

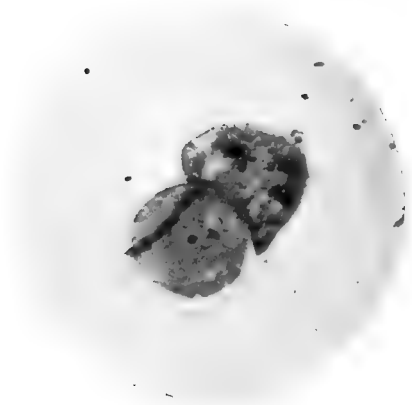


FIG. 3.





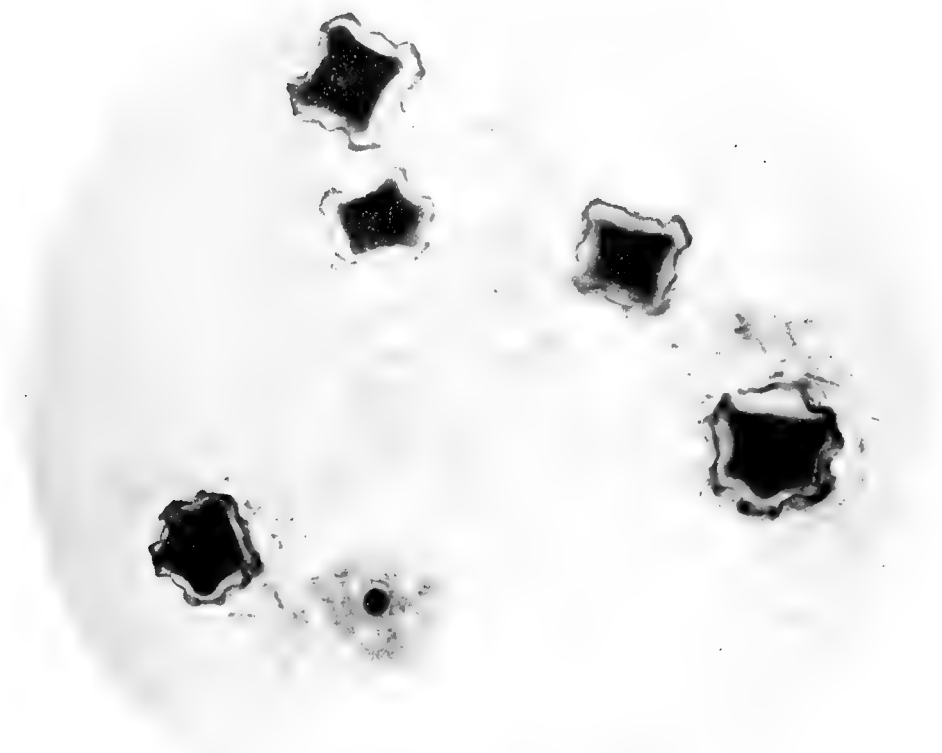


FIG. 4.

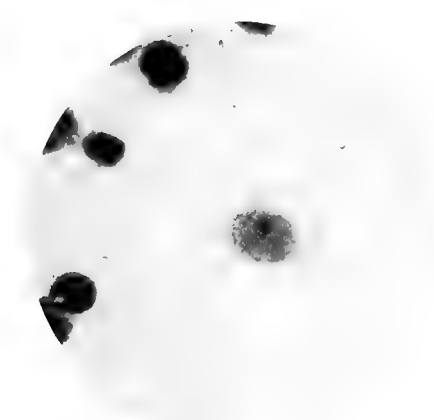


FIG. 5.

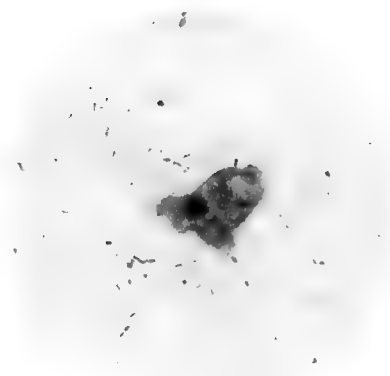


FIG. 6.



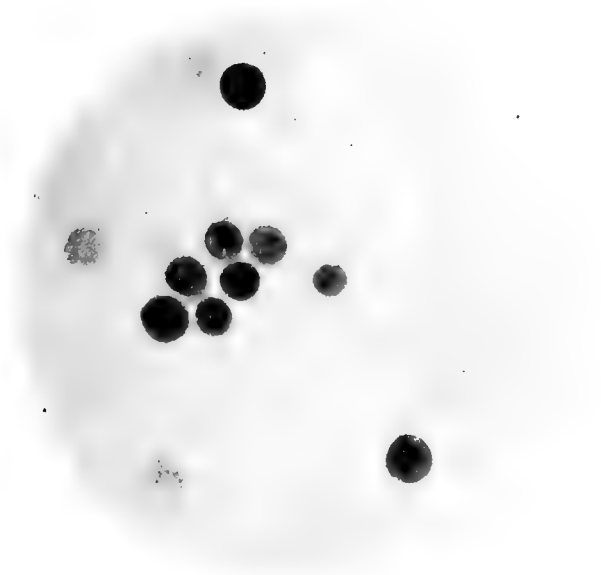


FIG. 7.



FIG. 8.

PLATE III.



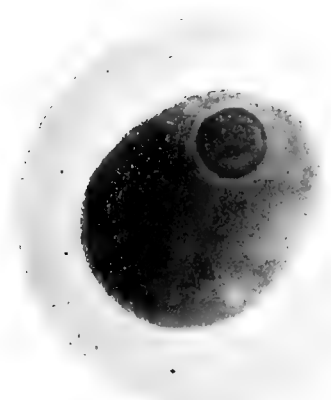


FIG. 9.

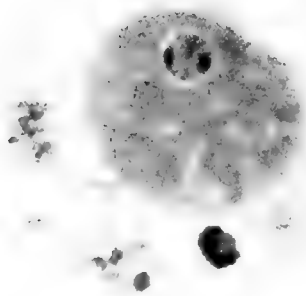


FIG. 10.

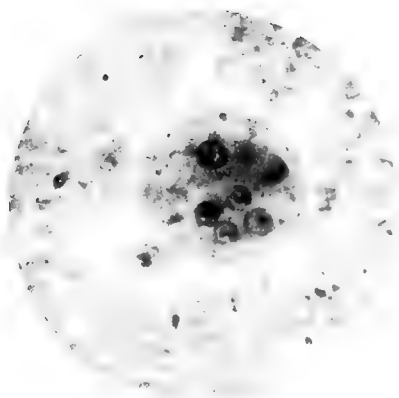


FIG. 11.

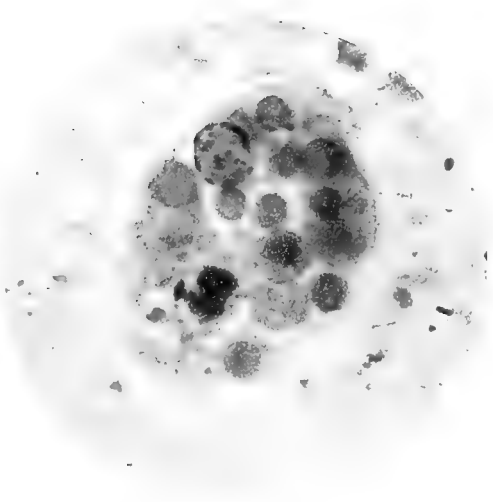


FIG. 12.

PLATE IV.



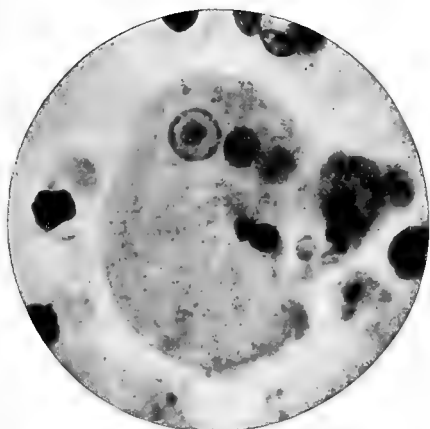


FIG. 13.



FIG. 14.

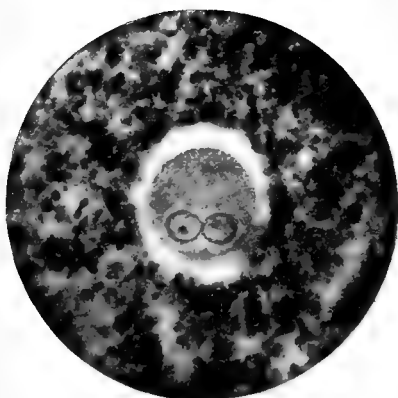


FIG. 15.

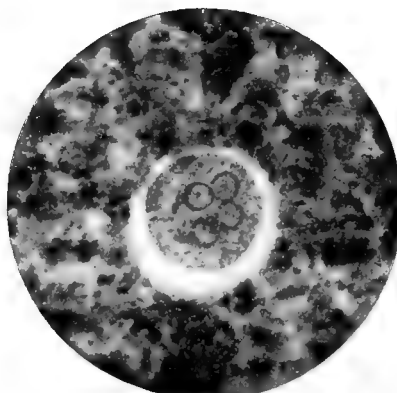


FIG. 16.

PLATE V.





## IMMUNITY REACTIONS WITH AMOEBÆ.

By ANDREW WATSON SELLARDS.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

The aetiology and also the diagnosis of amœbic dysentery involve the question of whether non-pathogenic as well as pathogenic amœbæ may be encountered in the human intestine. In the development of the evidence bearing upon this question, two factors have arisen which are of especial interest. In the first place important morphological differences have been described for amœbæ from various sources, and secondly cultures of amœbæ have been obtained from dysenteric stools. It is maintained that definite morphological distinctions occur in the amœbæ found in the intestine with differences in clinical manifestations corresponding to the type of amœba which is present. Thus, one of these types may persist over long periods of time without the production of definite symptoms. This fact appears to constitute the principal evidence in support of the existence of a non-pathogenic species of amœba in the intestine. However, the morphological differences between this type of amœba and that occurring in active dysentery have not been accepted by certain observers, and the existence of this type as a distinct species has been questioned.

In regard to the cultivation of amœbæ, there is some uncertainty concerning the exact significance of the cultures which have been obtained from dysenteric stools. Some investigators consider that the amœbæ in these cultures are pathogenic. Others regard them as purely saprozoic forms, which are only accidentally present in the fæces, maintaining that the morphological differences are sufficient to distinguish them absolutely from the amœbæ ordinarily seen in a dysenteric stool.

In the present paper an attempt has been made to distinguish amœbæ by their biologic properties without especial reference to morphology. Immunization of animals has been carried out with various strains of amœbæ with the expectation of producing immune bodies for the comparison of the various strains. It was intended, in the first place, to determine whether any differences could be detected in the immunity reactions of cultures of amœbæ obtained from parasitic as compared with those from saprophytic sources. In the second place, the sera of dysen-

teric patients have been examined for changes analogous to those produced by artificial immunization with amœbæ. The number of cultures under investigation was limited to four and these were selected, without regard to morphology, from sources which represented fairly distinct conditions.

The first culture, Race A,<sup>1</sup> was obtained from the city water supply of Manila. This is an unfiltered river water which comes, however, from a practically uninhabited watershed. Amœbæ are constantly present in this water. Race B. was cultivated from the stools of a case of amœbic dysentery occurring in Manila. The two remaining cultures were secured from sources outside of the Tropics. Race C. was grown from hay obtained from central Illinois, a region practically free from amœbic dysentery. Race D. was cultivated in Kansas City, from the stools of a patient with slight diarrhœa.

In the preparation of these cultures for injection into animals, there are two factors which were considered to be of especial importance, namely, (1) the isolation of a single species of amœba and (2) its cultivation with a single species of bacterium.

Much of the morphologic work upon amœbæ has been carried out upon material which might contain a variety of species but in attempting a differentiation by immunity reactions it seemed especially desirable to isolate single species of amœbæ, i. e., to know that each culture consisted of the progeny of a single organism.

The most feasible method for the isolation of single cells is that devised by Barber(1) and it is readily applicable to amœbæ. In transferring single motile amœbæ from cover glasses and pipettes to nutrient media they exhibit some tendency to stick to the glassware in a manner similar to certain cells, such as leucocytes and some of the capsulated bacteria. The cysts of amœbæ, do not possess this characteristic and they can be isolated and transferred readily. Accordingly, the isolations were first attempted with the encysted stage. However, it was found that only a small proportion of the isolated cysts would multiply when transferred to agar, prepared for the cultivation of amœbæ. The substitution of a liquid, nutrient medium for the agar would reduce the manipulations to a minimum, thereby permitting the isolation of organisms in the amœboid stage without necessitating further transference in order to supply nutrient material. Normal rabbit serum was found to constitute a suitable liquid culture medium. Emulsions of motile amœbæ were prepared in serum in dilutions varying from 1 to 5 to 1 to 10 and the isolations were made immediately in hanging drops on cover slips. The entire drop was not too large to come within the field of the one-sixth or one-twelfth objective. The fluid medium was quite clear and accordingly it could be determined definitely when a single amœba was obtained. In order to supply an abundance of nutrient material the size of the droplet was increased, after isolation was effected, to a diameter of 1 or 2 millimeters. Under these conditions, multiplication took place in about one-fourth of the isolations. In the remaining three-fourth the amœbæ disintegrated, encystment rarely taking place. The hanging drop cultures were kept both at

<sup>1</sup> These cultures have been designated simply by letters, in as much as the basis for the classification of amœbæ into species is incompletely developed and the description of the various species which have been reported is often inadequate for their identification.

room temperature (about 25° to 30° C.) and incubator temperature (37° C.); either was found to be satisfactory. Within the first 48 hours as many as 10 to 20 organisms usually developed from the original parent cell. The drop was then transferred with a comparatively coarse pipette to agar media and the cultures were continued in the usual manner.

One race (D) had already been isolated from a single cell before it was received at the laboratory. This culture was obtained by Professor M. A. Barber of the University of Kansas from the fæces of a patient with a watery diarrhœa. Individual cysts were selected and isolated directly from the fæces. Upon transferring to nutrient media, some of these cysts developed, thus not only giving a culture consisting of a single species of amœba but also demonstrating that the cyst-like bodies seen in the fæces were true amœbæ.

The presence of bacteria in the cultures of amœbæ<sup>2</sup> naturally necessitates a considerable number of controls in the study of the immune bodies resulting from the injection of these mixtures. To simplify these controls, somewhat, the four different races of amœbæ were cultivated with the same species of bacterium. *B. prodigiosus* was chosen, since amœbæ grow well in conjunction with it and its chromogenic properties simplify the detection of contaminations by other bacteria. As a further control, one of the races of amœbæ was also cultivated with *Vibrio cholera*. The separation of amœbæ from all of the accompanying bacteria except one species was found to be rather difficult. Even in the encysted stage, the amœbæ are in general rather less resistant to physical and chemical agents than the sporeforming bacteria which occur with them. In the motile stage, they are intimately mixed with bacteria, the latter clinging to the surface and also being enveloped in the substance of the amœbæ, while the spores may resist any digestive action.

The method devised by Mouton(3) was used for obtaining the amœbæ in culture with a single species of bacteria. The center of a Petri plate was inoculated with amœbæ, the desired bacterium having been inoculated previously in lines radiating from the center. As the amœbæ wandered over the plate they followed the lines of bacterial growth, gradually leaving the contaminating bacteria behind them. After several transplantations had been made in this manner, test tubes were substituted for Petri plates to avoid accidental contamination from the air. The entire surface of an agar slant was inoculated with bacteria, the inoculation of the amœbæ being made at the base of the tube. After 24 hours in the incubator with the tubes placed in the erect position, the amœbæ grew upward a distance of 3 to 5 centimeters, a sharp line of demarcation frequently appearing at the junction of the growths of the bacteria and the amœbæ. Many repetitions of this process were necessary before all of the con-

<sup>2</sup> Many of the earlier observers have attempted to obtain pure cultures of amœbæ, but no successful method was established whereby development continues indefinitely in the absence of both living and dead bacteria. However, very recently, Williams(2), in a preliminary communication, reports successful cultivation in the absence of bacteria.

taminating organisms were eliminated. It was a comparatively simple matter to obtain an apparently pure culture of bacteria, but more extended observations often revealed the presence of contamination. Thus minute quantities of a culture when plated out for development of single colonies frequently showed nothing but *B. prodigiosus*, while in the course of a few weeks, other bacteria might appear in the original culture, although it had been carefully protected from contamination. It is to be noted that the culture of *prodigiosus* lost its power of producing pigment on the amœbæ agar, but this property was at once regained on the first transplantation to ordinary agar. In the isolation of amœbæ with *Vibrio cholerae*, a culture was readily obtained which showed only cholera colonies when small quantities were inoculated on ordinary agar. However, the inoculation of a large quantity of growth into a highly active anti-cholera serum resulted in the destruction of practically all of the cholera organisms and a spore-forming bacillus developed in the serum.

The stock cultures of amœbæ were always kept in test-tubes. Bacteria were added at practically every transfer and the inoculations were made in the same manner as for the purification of the cultures; that is, the entire surface was inoculated with *B. prodigiosus*, but only the base of the slant with amœbæ.

*Technique of cultivation.*—The majority of the various media for amœbæ depend upon the same principle, namely the reduction of the nutrient material to such a minimum that only a scanty development of bacteria can take place. Thus, there are the dilute liquid media such as the hay and straw infusions; the solid medium of Beyerinck(4) is prepared with agar which has been repeatedly extracted with water; the alkaline agar of Musgrave and Clegg(5) contains 0.03 to 0.05 per cent of beef extract and no peptone. An agar based upon the last formula was used for maintaining the stock cultures of amœbæ. The principal difference consisted in the reactions of the media, the final product when ready for inoculation being neutral to phenolphthalein. The following formula was used: Agar-agar 2.5 per cent, Liebig's beef extract 0.05 per cent, normal sodium hydroxide 2 per cent. This medium, without clarification, was sterilized at 7 kilograms pressure per square centimeter for three-fourths of an hour. After sterilization it was found that the reaction of the medium was neutral to phenolphthalein, the alkali presumably having combined with the organic material in the agar. Furthermore, under these conditions of temperature and duration of heating, the quantity of alkali which was sufficient to render the medium permanently alkaline was slightly in excess of the amount which was sufficient to prevent the agar from solidifying at room temperature. Nevertheless, although the reaction of the medium was ultimately neutral, to phenolphthalein the addition of the excess of alkali gave a better medium for the cultivation of amœbæ than was afforded by the use of agar which was just neutral or slightly alkaline before sterilization.

On agar media of the ordinary composition with an acid reaction such as are used for bacteria, no growth of amœbæ could be obtained, although some investigators have used such a medium successfully.(6) Under certain conditions, when it was desired to obtain amœba-free cultures of bacteria which were associated with amœbæ, ordinary agar was used, the first transplantations being free from amœbæ.

With the development of the methods for the cultivation of amœbæ, solid agar media have largely replaced the liquid media which were used by the earlier workers. Although straw infusions and similar fluids have been used in obtaining amœbæ for study, their isolation and propagation has been carried out chiefly on solid media. It has even been stated that, with many amœbæ, direct

inoculation from solid to liquid media is difficult or impossible.<sup>(5)</sup> However it was found that some of the ordinary liquid media were very suitable for the cultivation of amœbæ, provided that these media were first diluted to such an extent that the growth of bacteria was considerably restricted. Thus, amœbæ grew well in a solution of 1 part of peptone in 1000 parts of water and fair growth occurred in ordinary nutrient bouillon when diluted to 1 part in 100, although no growth of amœbæ took place in a 0.5 per cent solution of peptone, or in bouillon of the ordinary strength. There was a fairly wide range in the concentrations of peptone which were found suitable, abundant growth taking place in dilutions varying from 1 part in 1,000 to 1 in 5,000. The amœbæ could be transferred backward and forward from the solid to the liquid media, a good growth being obtained on the first inoculation, in the same manner as with bacteria.

Occasionally, after cultivating a species of amœba for several months on the medium containing agar and beef extract, the composition was altered slightly for one or two generations by the substitutions of 0.1 per cent peptone and 0.05 per cent lactose for the beef extract. Sometimes, when the growth on agar became less abundant, a few transplantations were made in liquid media, using either diluted normal rabbit serum or a solution containing 1 gram of peptone and 0.5 gram of lactose in 1,000 cubic centimeters of water. As a general rule, the most abundant growths of amœbæ were obtained at incubator temperature (35° C.).

One well marked exception was found to the apparent necessity of a highly diluted medium for the growth of amœbæ. All of the four cultures of amœbæ grew well in normal serum not only when it was highly diluted but also in the lower dilutions. Thus, excellent growth took place not only in dilutions of 1 to 500, but also in 1 to 2, and in 1 to 5. This ability to develop in normal serum was utilized later in testing for the production of immune sera.

*Technique for immunization.*—The cultures of amœbæ on agar slants were used for the inoculation of animals. Living organisms were injected in the amœboid condition, emulsions being prepared in water from 24-hour cultures. The amœbæ which were used for injection, were always grown with *B. prodigiosus*. No attempt was made to reduce the quantity of bacteria in the mixed emulsion of amœbæ and bacteria, but when care was taken to insure favorable conditions for a vigorous growth of amœbæ, the latter always predominated to a considerable extent over the bacteria.

Rabbits were used for immunization. The first two injections and sometimes the third were made intravenously and the remaining ones intraperitoneally. The injections were made at intervals of ten days to one month according to the condition of the rabbits, and the maximum period of treatment for any one animal was thirteen months. For rabbits weighing about 1.5 kilograms, one-half to one agar slant of the ordinary size, (measuring about 1.5 by 8 centimeters) upon intravenous injection was usually fatal within 12 to 18 hours. Under the same conditions, 2 slants were usually fatal upon intra-peritoneal injection. Several rabbits were used for each of the 4 cultures and varying quantities of material

were injected. As a rule one-eighth to one-fourth of an agar slant was used for the first injection and this was gradually increased to 6 or 8 slants. Perhaps the best result was obtained in a rabbit which at the first injection survived 1 agar slant given intravenously. Pronounced symptoms occurred; within 6 hours the rabbit became semi-comatose, the temperature rose from 39°.5 C. to 40°.1 C. and the respiratory and heart rate were too rapid to count. This rabbit received subsequent injections of amœbæ without loss of weight, or other symptoms and was eventually able to withstand 20 agar slants intraperitoneally at a single injection. Five other rabbits receiving a similar injection died within 15 hours.

The preceding technique has been observed as a routine, but other animals and other methods were also tested. Thus one series of guinea pigs was injected with cultures killed by heating to 50° C. for fifteen minutes. Whereas guinea pigs, upon intra-peritoneal injection, were able to survive only a small oese of living amœbæ as much as 1 agar slant of a killed culture could generally be used for the first injection and as many as 4 or 6 slants could be used in rabbits; however, the formation of immune bodies was not active and the subsequent injection of living amœbæ was not borne very much better than when the first injections were made with smaller quantities of the unheated material.

In one rabbit, the organisms were injected only in the encysted stage, viable cysts being given intravenously for the first two injections and the remaining injections being made intraperitoneally. This rabbit was used only in testing for agglutinins.

In as much as antibodies form readily upon the injection of vegetable cells, of animal tissues, and of unorganized protein matter, and since they occur in natural infections with protozoa, it would be expected, *a priori*, that amœbæ would also act as antigen. No attempt was made to investigate all of the immunity reactions which might be produced with amœbæ, but rather I have sought to obtain a reaction which would be suitable for distinguishing cultures from various sources. Accordingly, preliminary tests were carried out with only one of the cultures of amœbæ (Race A). Of the commoner biological reactions those for agglutinins, precipitins, cytolytins, and anaphylaxis have been considered.

*Agglutination.*—Agglutination tests were carried out on both the active and the encysted stages of amœbæ with serum obtained, first, from guinea pigs and rabbits injected with the motile amœbæ and second from a rabbit injected with encysted forms. In the amœboid stage, some difficulty was encountered in securing a uniform suspension of the organisms in the control preparations. The immune sera from rabbits and guinea pigs were tested in varying dilutions up to 1 in 1,000. In hanging drops, irregular clumping sometimes occurred in portions of the prep-

aration, but differences from the control were neither constant nor well defined. In the encysted stage, uniform emulsions for agglutination were readily obtained. The serum from a rabbit which had been treated with cysts for 3 months proved to be entirely inactive. Also, the serum from rabbits treated with organisms in the amœboid stage showed no agglutinative action toward the encysted stage.<sup>3</sup>

*Precipitins.*—Examination for precipitins was somewhat complicated, partly because of the difficulty of securing a suitable extract of amœbæ and also on account of the controls rendered necessary by the possibility of the presence of bacterial precipitins.

An extract of amœbæ grown with *B. prodigiosus* was prepared by emulsifying the growth from 24-hour agar slants in the water of condensation and grinding this emulsion with sand. The fluid was collected by centrifugalization and clarified by filtration. A clear filtrate was obtained most readily by the use of a Berkefeld filter, but the precipitation reactions were more satisfactory when the extract was filtered through magnesium oxide. Serum from a rabbit which had been under treatment for five months gave a well marked precipitation in 1 to 2 and 1 to 5 dilution with the undiluted extract from the mixture of amœbæ and *B. prodigiosus*. However, this same extract also gave a precipitate with the serum from a rabbit treated with *B. prodigiosus* alone. In order to control the effect of bacterial precipitins, an extract of amœbæ growing with *V. cholerae* was tested against the serums of a rabbit immunized to amœbæ growing with *B. prodigiosus*. Only a poorly defined precipitate was obtained in 1 to 2 dilution of serum from animals which had been under treatment for from two to five months. These preliminary results, therefore, did not indicate that precipitin tests would afford a very suitable reaction for the study of amœbæ, both on account of the technical difficulties and also because of the indefinite reactions which were obtained.

*Anaphylaxis.*—The usual test for anaphylaxis with death of the animal requires rather more material than conveniently can be obtained from cultures of amœbæ. However, the intradermal reaction as devised by Knox Moss and Brown,<sup>(8)</sup> would be especially serviceable for work with amœbæ. Rabbits and guinea pigs were tested within two to four weeks after the first injection and also at later periods after treatment had been continued for from 1 to 6 months. The injections were made intradermally with amœbæ growing with *B. prodigiosus*. Two preparations of amœbæ were used. One consisted of an extract, filtered through magnesium oxide in the same manner as for the precipitin test. The other

<sup>3</sup> However, successful agglutination of amœbæ by a non-specific serum, has been reported by Zaubitzer<sup>(7)</sup> who found that the serum of an animal when immunized to *V. cholerae*, agglutinated amœbæ growing with *V. cholerae*.

was merely an emulsion of a 24-hour culture in physiologic salt solution. No well defined differences were obtained between the injections in normal animals and those injected with amœbæ and *B. prodigiosus*. The bleb produced by the injection was usually absorbed within the course of an hour. After 12 to 18 hours some cedema and reddening appeared at the site of injection. This was distinctly more marked in the cases where an unfiltered extract of amœbæ was used, suppuration eventually resulting in some instances. The differences between the normal animals and the treated ones were slight and inconstant. However, the general tendency of such differences as were noted, was not in the direction of a greater reaction in the treated animals, but on the contrary these animals sometimes showed signs of less inflammation at the site of injection than the controls. The differences, however, were altogether inadequate for any satisfactory test and attention was next given to cytolytins.

*Cytolytins.*—Tests for the cytolytic action of the sera were carried out microscopically. Ordinary hanging-drop preparations were made from equal parts of a suspension of amœbæ and immune serum. The suspension of amœbæ was prepared in the water of condensation from the agar culture media, in preference to normal physiologic salt solution, since the latter is hypertonic for amœbæ. A certain amount of salt could be used to advantage, perhaps, imitating the conditions which occur in surface waters, the natural habitat of some of these amœbæ, but in attempting to determine the most desirable amount of salt it was found that the amœbæ when transferred from agar to distilled water showed no definite morphologic change and remained in the amœboid stage for at least several days. The serum dilutions also were prepared with water, and not with salt solution.

In testing for cytolytins, control preparations were made with normal serum, with physiologic salt solution, and with distilled water. Slight changes were noticeable immediately after preparing the mixtures. Some of the amœbæ lost their motility and assumed a spherical form, both in the preparations with immune serum and also to a lesser extent in those with normal serum and with physiologic salt solution, while in those with distilled water, no change was observed. With immune serum of a high grade cytotoxicity of the amœbæ could be observed microscopically and in the course of one to two hours there was a well marked diminution in the number present in the hanging drop. Sera which were sufficiently active to cause immediate cytotoxicity were obtained only with some difficulty and after a comparatively long period of immunization. Furthermore, none of the preparations showed complete cytotoxicity of all of the amœbæ present, the differences between the normal and immune serum in this



respect being only relative and not absolute. However, after 24 hours at 35° C. a definite result was readily obtained, notwithstanding the fact that rabbit serum in 1 to 2 dilution furnishes a good culture medium in which a few surviving amœbæ might develop. In the mixtures with distilled water and normal serum the amœbæ remained actively motile without any encystment before the second or third day and without any significant change in numbers. No increase in number was to be expected since the concentrations of the amœbæ in the suspension was usually greater than that which occurs in liquid culture media. In the test preparations with serum from treated animals the reaction was usually very definite. Either there were many motile amœbæ present just as with normal serum, or else there was almost a complete lysis of the amœbæ with only a few cysts and an occasional motile organism present. Occasionally, in the preparations with immune serum, many of the amœbæ took on a pink color. This was due apparently to the presence of granules of *B. prodigiosus*, although no color was visible in the suspension of bacteria surrounding the amœbæ.

The reaction in this form was then adopted for testing the behavior of the 4 races of amœbæ. The suspension of amœbæ was always prepared in the water of condensation, from an actively growing 24-hour culture in the amœboid stage. Equal parts of this suspension and the serum to be tested were mixed with a capillary pipette according to Wright's technique and a hanging drop preparation was made from a portion of the mixture. In order to obtain constant and well defined reactions, it is necessary that the amœbæ in the culture should be abundant and should predominate over the bacteria present. The data which follow represent the conditions of the preparations after standing for eighteen to twenty-four hours at 35° C. The concentrations of serum are expressed in the final concentration after dilution with the suspension of amœbæ, for example, 1 part of undiluted serum and 1 part of the suspension is recorded as a 1 to 2 dilution of the serum.

On account of the presence of bacteria throughout the entire procedure there are several interpretations which might be considered with regard to the cause of the destruction of the amœbæ by the immune sera. Three general methods were used for detecting the effect of the bacteria. The serum of rabbits immunized to amœbæ in mixed culture with *B. prodigiosus* was tested against a culture of amœbæ growing with *B. prodigiosus* and with *V. cholera*. Also, the serum of a rabbit immunized to *B. prodigiosus* alone was tested against a culture of amœbæ growing with *B. prodigiosus*. These controls were carried out with the culture designated A and the results of the first and second methods appear in Table I.

TABLE I.—*Production of cytolytins by injection of amœbæ in mixed culture with B. prodigiosus.*

Serum of rabbit immune to—	Agglutination of <i>B. prodigiosus</i> —				Lysis of amœbæ in cultivation with—			
	In pure culture at dilution of—		In mixed culture with amœbæ at dilution of—		<i>B. prodigiosus</i> at dilution of—		<i>V. cholerae</i> at dilution of—	
	Experi- ment I.	Experi- ment II.	Experi- ment I.	Experi- ment II.	Experi- ment I.	Experi- ment II.	Experi- ment I.	Experi- ment II.
<i>B. prodigiosus</i> -----	1-50	1-100	1-50	1-50	{None. 1-2	None. 1-2	None. 1-2	None. 1-2
Amœbæ and <i>B. prodigiosus</i> -	1-5	1-5	1-10	1-5	1-5	1-10	1-5	1-5
Control, normal rabbit	{Slight.	None.	None.	None.	None.	None.	None.	None.
serum -----	1-2	1-2	1-2	1-2	1-2	1-2	1-2	1-2

From these data it appears that the lysis of the amœbæ was due to the immune bodies formed in response to the injection of the amœbæ, and not to the accompanying bacteria, since the amœbæ growing with cholera were acted upon by the serum produced by the injection of amœbæ and *B. prodigiosus*, whereas the serum produced by the injection of *B. prodigiosus* alone was inactive for amœbæ. In the comparison of the different races of amœbæ it will be seen that there is some additional evidence in support of the preceding conclusions.

The activity of the serum is of extremely low grade even for protozoan material. The highest serum which was obtained at any time was that from a rabbit which had survived on the first injection 1 agar slant of amœbæ. The same dose was fatal for 5 other rabbits. Five months after the first injection, when the rabbit was able to withstand 4 agar plants intraperitoneally at one injection, the serum was found to be active in 1 to 50 dilution. This degree of activity persisted for only 2 days and then fell to 1 to 10; subsequent injections failed to increase it. Apparently, the repeated injections of amœbæ instead of producing highly active sera only caused the low grade of activity to persist over longer periods. In considering the degree of activity which was obtained, it is to be noted that the amounts of material injected were rather lower than are ordinarily used in working with animal cells, such as red blood corpuscles. The quantities used were probably not as great as are usually employed for many of the ordinary bacteria such as *V. cholerae* or *B. typhosus*. Two factors were concerned in producing this limitation, namely the relatively small quantity of amœbæ which can be obtained from the growth on agar and the inability of animals to withstand the injections, emaciation and death resulting from an over dosage.

*Character of the immune bodies.*—A few tests were made to determine whether the destruction of the amœbæ was accomplished by the combined action of amboceptor and complement in a manner analogous to the action of hæmolysins and bacteriolysins. The effect of heating is shown by the results in Table II. The serum of a rabbit immunized to amœbæ (race A) and *B. prodigiosus* was tested against the same mixture of amœbæ and bacteria. One part of serum was diluted with 1.5 parts of water for the purpose of heating at 70° and 78°.

TABLE II.—Showing effect of heat on immune serum.

Lysis produced by heated immune serum.	Dilution of immune serum.	Temperature and duration of heating.					Unheated immune serum.
		60°, one-half hour.	60°, 1 hour.	60°, 3 hours.	70°, one-half hour.	78°, one-half hour.	
With complement added:							
Normal rabbit serum—							
1 to 10 -----	1-2	Active.	Active.	Active.			
	1-5	Active.	Active.	Active.	Active.	Active.	
	1-10	None.	None.	None.	None.	Slight.	
1 to 5 -----	1-2	Active.	Active.	Active.			
	1-5	Active.	Active.	Active.	Active.	Active.	
	1-10	None.	None.	Slight.	None.	Slight.	
Without comple- ment -----	1-2	Active.	Active.	Active.			Active.
	1-5	Active.	Active.	Active.	Active.	Active.	Active.
	1-10	None.	None.	Slight.	Slight.	Slight.	Slight.

This activity of the serum after exposure to relatively high degrees of temperature seems at first a little unexpected. However, related phenomena have been observed with other protozoa and even with bacteria. Thus Rössle (9) found that an immune serum produced by the injection of paramœcia was not inactivated after exposure for 30 minutes to a temperature of 70° C. However Rössle does not describe this serum as a true cytolyisin and, furthermore, it was thermostable only when the injections were made with killed and not with living paramœcia. Laveran and Mesnil (10) found that an immune serum for trypanosomata was only partially inactivated after exposure to a temperature of 64° C for one-half to three-fourths of an hour. Later, Hamilton (11) reported a thermostabile bacteriolysin for an organism designated as the "Ruediger bacillus."

However, these results with amœbæ do not prove that the immune body is thermostable, unless normal heated serum also shows no activity. Accordingly, the effect of heat was tested both on normal serum and on the serum of a rabbit which had been immunized. This rabbit had formerly shown some immunity, its serum being active in 1 to 5 dilution. At the time of this test no injections of amœbæ had been given for 2 months and as seen in Table III, the unheated serum was inactive.

TABLE III.—*Lysis of amœbæ by heated sera.*

	Dilution.	Serum formerly immune to amœbæ.	Control, normal rabbit.
Control, unheated	1-2	None.	None.
	1-5	None.	None.
	1-10	None.	None.
Serum heated for one hour at—			
60° C	1-2	Active.	Active.
	1-5	None.	None.
	1-10	None.	None.
70° C	1-5	Active.	None.
	1-10	None.	None.
78° C	1-5	Active.	None.
	1-10	None.	None.

This result shows definite activity of the normal serum when heated at 60° and of the immune serum at 60°, 70°, and 78° C.

An additional test was carried out to determine whether this apparent difference between the normal and immune sera at higher temperatures is a specific property of anti-amœba sera or whether it is common to other immune sera. The sera of a rabbit immune to *V. cholerae* was used and a second rabbit formerly immune to amœbæ also tested in addition to the one used in the preliminary experiment. The results are given in Table IV.

TABLE IV.—*Lysis of amœbæ by heated sera.*<sup>4</sup>

	Dilution.	Serum formerly immune to amœbæ.		Serum immune to <i>V. cholerae</i> .	Controls, normal rabbit sera.	
		A.	B.		A.	B.
Control, unheated	1-2	None.	None.	None.	None.	None.
	1-5	None.	None.	None.	None.	None.
	1-10	None.	None.	None.	None.	None.
Serum heated for one hour at—						
60° C	1-2	Active.	None.	Active.	Active.	Active.
	1-5	None.	None.	None.	None.	None.
	1-10	None.	None.	None.	None.	None.
70° C	1-5	Active.	Active.	None.	None.	None.
	1-10	None.	None.	None.	None.	None.
78° C	1-5	Active.	Active.	None.	None.	None.
	1-10	None.	None.	None.	None.	None.

<sup>4</sup>The word lysis has been retained in speaking of the action of the serum on the amœbæ although the process, at least in the case of the heated normal serum, differs from that of the ordinary specific lysins. With an immune serum some solution takes place within the first few hours and although a period of eighteen or twenty-four hours may be required to complete the process, yet it is accomplished by a direct action on the amœbæ and it is not a secondary effect of the action of the antibacterial serum on the accompanying bacteria. Apparently the

In one instance in Table IV it will be noted that lysis of the amœbæ failed to occur in the 1 to 2 dilution of serum heated at 60° C. An emulsion was used which was unusually rich in amœbæ and, although the differences were well marked after the preparations had stood for 18 hours, yet the amœbæ did not entirely disappear until after 24 hours. These results might be taken as indicating that exposure to a temperature of 60° C. for one hour represents about the minimum time which would be effective in producing this change in the serum. Perhaps a more moderate heating might have inactivated the immune serum without producing this change which renders normal serum active. Although it is definitely shown that the immune serum is active after heating yet the controls with normal serum show that it does not necessarily follow that the immune bodies are thermostable or that they do not consist of amboceptor and complement. No attempt was made to work out the mechanism of this action of the heated normal serum. It is possible, of course, that it does not act directly upon the amœbæ, but affects them secondarily through a primary action on the bacteria; for example, the bacterial products formed in heated serum may be different from those in unheated serum. *Apriori*, however, the simplest explanation is that of a direct action upon the amœbæ. There is one instance in which heated normal serum can be shown to have a definite action on animal cells:

This phenomenon, which may be somewhat analogous to the reaction with amœbæ, can be demonstrated with red blood corpuscles<sup>5</sup> when heated normal serum develops the property of causing marked rouleaux formation of red corpuscles suspended in salt solution. The degree of heating which is required and the activity of the serum correspond rather closely to the conditions pertaining to amœbæ; thus, serum after exposure to 60° C. for 1 hour is effective in producing rouleaux in a final dilution of 1 to 4, but not in 1 to 6; normal serum after the same treatment is active toward amœbæ in 1 to 2 but not in 1 to 5 dilution. It may be noted that this action of heated sera in causing rouleaux formation is apparently only an increase of a normal characteristic of unheated sera. Similarly, it can be shown that although amœbæ grow well in a 1 to 2 dilution of normal rabbit serum, yet they are destroyed in undiluted normal serum, or in a 1 to 2 dilution of heated normal serum.

#### BIOLOGIC RELATIONSHIP BETWEEN THE DIFFERENT CULTURES OF AMŒBÆ.

The serum reactions with the 2 cultures of amœbæ obtained from saprophytic sources were compared with 2 cultures obtained from the intestinal tract to determine their identity or non-identity as tested by biologic methods. Rabbits were immunized in a similar manner to

term lysin is seldom applied to immunity reactions with protozoa. Rössle<sup>(8)</sup> observed that instead of lytic properties, cytotoxic sera often possess a paralyzing action; the examples cited are the spermotoxic sera, and the anti-sera against epithelium and against paramœcia.

<sup>5</sup> *Bull. Johns Hopkins Hosp.* (1908), 19, 271.

the 4 races of amœbæ, all of which were growing in conjunction with *B. prodigiosus*. Complete tests for the comparison of the 4 races of amœbæ were carried out simultaneously, using sera of a low grade but sufficiently active to give well-defined results.

The data for these tests are shown in Tables V and VI.

TABLE V.—*Biological relationship of the various cultures of amœbæ.*

[First determination.]

Serum.		Lysis of amœbæ.			
Immune to—	Dilution.	Race A.	Race B.	Race C.	Race D.
Race:					
A -----	1-2	Active.	None.	None.	Slight.
	1-5	Active.	None.	None.	None.
	1-10	Active.	None.	None.	None.
B -----	1-2	None.	Active.	None.	None.
	1-5	None.	Active.	None.	None.
	1-10	None.	Slight.	None.	None.
C -----	1-2	None.	None.	Active.	None.
	1-5	None.	None.	Active.	None.
	1-10	None.	None.	Active.	None.
D -----	1-2	None.	None.	None.	Active.
	1-5	None.	None.	None.	None.
	1-10	None.	None.	None.	None.
Normal rabbit serum-----	1-2	None.	None.	None.	None.
	1-5	None.	None.	None.	None.
	1-10	None.	None.	None.	None.
Control with water -----		None.	None.	None.	None.

TABLE VI.—*Biological relationship of the various cultures of amœbæ.*

[Second determination.]

Serum.		Lysis of amœbæ.			
Immune to—	Dilution.	Race A.	Race B.	Race C.	Race D.
Race:					
A -----	1-2	Active.	None.	None.	None.
	1-5	Active.	None.	None.	None.
B -----	1-2	None.	Active.	None.	None.
	1-5	None.	None.	None.	None.
C -----	1-2	None.	None.	Active.	None.
	1-5	None.	None.	Active.	None.
D -----	1-2	None.	None.	None.	Active.
	1-5	None.	None.	None.	Slight.
Normal rabbit serum-----	1-2	None.	None.	None.	None.
	1-5				
Control with water -----		None.	None.	None.	None.

It is clear from these tables that the 4 races of amœbæ are, biologically at least, distinct species, since the sera produced by them show a definite specificity. Here again it seems a little unusual that the first four races

selected should have reacted in absolutely different manners, not even group reactions being present. In Table V, the serum of race A apparently showed some activity against race D. Here it was thought that perhaps only a relative difference existed between the activity of serum A for amœbæ A and D, but subsequent tests did not confirm this view. In Table VI the difference is absolute and this result was confirmed by two subsequent tests. This behavior of the sera corresponds with the results obtained by Rössle<sup>(9)</sup> who found that the sera produced by paramœcia are also specific.

The specificity of the sera for the corresponding cultures affords additional evidence that the injections of the amœbæ were responsible for the activity of the sera, since it was possible for the amœbæ to vary in each culture, but the bacterial species, *B. prodigiosus*, was common to all. If any activity of the antibacterial serum against the *B. prodigiosus*, in the symbiotic culture of amœbæ and bacteria could have affected the growth of the amœbæ, then this effect should have shown itself in all four cultures.

A note on the morphology of these cultures is of interest in view of the biologic differences which were found. Dr. E. L. Walker of the biological laboratory, Bureau of Science, has very kindly examined these cultures and describes them as being readily distinguishable from each other on a morphologic basis, however all correspond to the *limax* type.

#### REACTIONS WITH SERA FROM DYSENTERIC PATIENTS.

The interpretation of these biologic differences requires some caution. Many possibilities present themselves in view of the failure of these amœbæ to fall into groups according to the source from which they were obtained. Thus any of these amœbæ may be pathogenic or any may be harmless. In the case of the cultures obtained from dysenteric fæces, it is possible that the pathogenic species may fail to grow on artificial media and the organism which does develop may be merely an accompanying saprozoite.

Accordingly, in an attempt to determine whether these amœbæ bear any ætiologic relationship to amœbic dysentery, these four races were tested against the sera of amœbic dysentery patients. In considering the possibility of the formation of immune bodies during the course of the disease it is of some interest to note whether there is any indication of the absorption of toxic products from the intestine which might serve as antigen. In the first place, it is note-worthy that there is some opportunity for such absorption since the amœbæ penetrate deeply, in large numbers, into the submucosa of the intestine. Second, changes in the formed elements of the blood are known to occur, a leucocytosis sometimes being present involving not only the polymorphonuclear neutrophiles but in some instances the mononuclear neutrophiles and the eosinophiles as well. Also, in severe infection some fever is often present. Perhaps the most favorable cases for the absorption of antigen and the production

of immune bodies would be those in which infection of the liver with abscess formation has occurred. However, one would not expect to find very active sera in view of the low grade of immunity in protozoan infections generally and because of the comparatively slight response of animals to the injections of amoebæ.

Samples of sera were taken in the stage of active dysentery, during convalescence, and after recovery, the majority of cases having been treated with ipecac. The diagnosis of the cases was based upon the presence of a dysentery resembling the usual course of the amoebic type together with the finding of amoebæ microscopically in the stools. No cases were available in which spontaneous recovery took place, although some had experienced repeated relapses alternating with periods of several months in which no symptoms were present.

The sera from these cases were tested against the 4 races of amoebæ. As a routine, the serum was used in dilutions of 1 to 2, 1 to 5, 1 to 10, 1 to 20, 1 to 50, and 1 to 100, the final readings being made after 18 to 24 hours. In the first case which was tested, the sample of serum was taken 4 days after the subsidence of an acute attack of dysentery. A definite reaction took place at 1 to 2 dilution with Race A, the amoebæ obtained from the city water supply. The preparations in the other dilutions and with all of the other amoebæ behaved like the controls prepared with normal serum. In a repetition of this test 4 days later, no reaction was obtained in any dilution with any of the 4 races of amoebæ. The second patient who was examined had exhibited symptoms of chronic dysentery for many months. The serum from this case reacted only in 1 to 2 dilution with Race B, the amoebæ cultivated from the stools of a dysenteric patient. All of the other preparations showed no lysis. There was no opportunity for confirming this result. The remaining cases that were examined consisted of 5 acute cases, 8 chronic ones, and 3 with liver abscess. The acute cases were examined while the symptoms were active and also within two to four weeks after recovery. None of these reacted with any of the races of amoebæ that were tested. The 8 chronic cases were examined during a period of relapse and 5 of these were also tested at a later period when they were free from symptoms. All, however, reacted like the normal control sera, the amoebæ remaining numerous and active in the 1 to 2 preparations and in all of the higher dilutions. Of the 3 cases of amoebic abscess of the liver, one was tested 4 days before exitus and the other two were tested at operation and after recovery. The sera of these cases produced no lysis with any of the cultures of amoebæ, and these cultures failed to agglutinate with the sera from the human cases.

From the behavior of these tests, it seems probable that the reactions obtained in the first 2 cases were merely accidental. The reaction resulted in one case with amoebæ secured from a well-protected river-water,



and in the other with amœbæ cultivated from a dysenteric stool. In both instances, the tests were carried out at a time when the cultures were growing only moderately well. Both reactions were obtained in 1 to 2 dilution and it is not unlikely that the absence of amœbæ is to be accounted for by the excessive growth of bacteria.

In as much as these tests failed to show any evidence of immunity, it seemed desirable to carry out some of the reactions with amœbæ known to be pathogenic, and to this end an attempt was made to utilize dysenteric stools in which the amœbæ were very numerous. The serum reaction as used with cultures of amœbæ, requires some modification in applying it to a dysenteric stool, since the amœbæ disintegrate within a few hours in the stool itself, or in any ordinary culture medium. Accordingly, mixtures of stools containing numerous amœbæ and the sera from dysenteric patients were made in the same manner as for cultures of amœbæ to determine whether any changes would take place within a few hours, before the control preparations deteriorated.

Two patients were selected in which the stools consisted largely of blood and mucus, practically free from faecal matter and in which the amœbæ were numerous in every field. Equal parts of these stools were mixed, first with the undiluted sera from the corresponding patients; second, with the serum from a case with acute symptoms of dysentery; and third, with serum from a patient who about three weeks previously had recovered from an acute attack of dysentery. Control preparations were made from normal serum. The amœbæ remained alive and active for a period of 2 hours. At the end of 3 hours the motility was much diminished in all preparations and the amœbæ were disintegrating in the preparations with the sera of dysenteric cases and in the control preparations as well. Further work upon the aetiology and diagnosis of amœbic dysentery by immunity reactions did not appear to be feasible on account of the lack of cultures known to be pathogenic.

#### SUMMARY.

The injection of cultures of amœbæ into rabbits resulted in the production of serum which was cytolytic for amœbæ.

This serum possessed only a low grade of activity. No inactivation resulted after exposure to a temperature of 60° C. for periods varying from thirty minutes to three hours or 70° C. for thirty minutes. However, the anti-bodies of the serum were not proved to be thermo-stable, since normal serum became active when heated for one hour at 60° C.

Of the sera produced by 4 cultures of amœbæ obtained from parasitic and from saprophytic sources each serum was cytolytic for the corresponding culture, but not for the other three. This specificity indicates that these amœbæ are biologically distinct. Subsequent examination showed

that these amœbæ are also distinguishable from each other upon a morphologic basis.

Examination of the sera of amœbic dysentery patients failed to demonstrate any production of immune bodies for amœbæ during the course of the disease. However, the method which was employed was not satisfactory when applied directly to amœbæ occurring in bloody mucus stools. Consequently, the results do not represent any reaction upon amœbæ which are known to be pathogenic. Tests upon cultures of amœbæ did not give any definite evidence of the presence of either cytolisins or agglutinins in the patient's serum.

Unfortunately these results do not lead to any definite conclusion but merely indicate that either immune bodies were not produced or that the cultures under consideration do not bear any ætiologic relationship to amœbic dysentery. Certainly there is no evidence of pathogenicity; however, on the other hand, there is nothing but negative evidence indicating their harmlessness.

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# TYPHOID FEVER IN THE PHILIPPINE ISLANDS.

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By WESTON P. CHAMBERLAIN.<sup>1</sup>

(*From the United States Army Board for the Study of Tropical Disease as they Exist in the Philippine Islands.*)

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PART I. PREVALENCE AND DISTRIBUTION OF TYPHOID FEVER IN THE PHILIPPINES.

PART II. LABORATORY INVESTIGATIONS OF TYPHOID FEVER IN THE PHILIPPINES.

PART III. CLINICAL ASPECTS OF TYPHOID FEVER IN THE PHILIPPINES.

PART IV. A STUDY OF RECENT TYPHOID EPIDEMICS IN THE PHILIPPINES.

PART V. CONCLUSIONS.

PART I. PREVALENCE AND DISTRIBUTION OF TYPHOID FEVER IN THE PHILIPPINES.

## INTRODUCTION.

From December 1, 1908, to date of this writing (April 30, 1911) the Board for the Study of Tropical Diseases has been making for the Philippines Division the routine blood cultures and Widal examinations on the military patients suspected of having typhoid fever and, also, making for convalescents the cultural examinations of the stools and urine which are required before a soldier who has had typhoid is allowed to return to duty. For nearly all cases in which we obtained positive laboratory findings a clinical history has been furnished to the Board. From this laboratory and clinical material we have been able to learn much of interest as regards typhoid in the Philippine Islands.

The greater part of our material for blood culture comes from a considerable distance, the time consumed *en route* varying from a day to several weeks. The same applies to the stool and urine specimens, and, furthermore, these excretions are not sent for diagnostic purposes but only to determine that the convalescent is not a bacillus carrier. Therefore, the cultural examinations in a large proportion of our cases are negative. It follows that for diagnostic purposes we must depend mainly on the serum reaction. Recently antityphoid

<sup>1</sup> Major, Medical Corps, United States Army, president of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

vaccination has been coming into quite general use among the American troops. As is well known, a typhoid vaccination will cause a positive Widal reaction, and of late it has been becoming obvious to us that the more general use of antityphoid vaccination would largely vitiate any deductions in the future which could be drawn from positive Widal reactions in fevers of doubtful nature. For this reason we have decided to compile the results of our work to date, the possibility of typhoid vaccination having been excluded in all of the cases referred to below.

While several articles from the pens of different authors have appeared on certain typhoid epidemics in the Philippines, (11) (12) (15) nothing, so far as we are aware, has been written which gives a comprehensive view of the typhoid situation throughout the Archipelago. Therefore, we feel that such a report can not fail to be of value to those interested in the sanitary problems of the Philippines.

#### TYPHOID IN THE TROPICS.

Typhoid fever, although not classed as a tropical disease, nevertheless is one which is of great interest and importance to those practicing in warm countries where it should always be born in mind when the physician is confronted by a patient with any febrile disturbance.

Manson says: "The existence of typhoid fever in the tropics was for long not only ignored but actually denied, even by physicians and pathologists of repute."<sup>(1)</sup> Malaria has been the scapegoat for the diagnostic shortcomings of the tropical practitioner. At the present day it is quite generally conceded that typhoid is a common disease among white men resident in low latitudes and that it is alarmingly prevalent among young Europeans in many parts of the tropical Orient. Castellani<sup>(2)</sup> and Rogers<sup>(3)</sup> agree with Manson in this opinion. Rogers found that among Europeans born and bred in the Tropics the incidence of the disease was especially marked in children under 15 years of age.

As regards the occurrence of enteric fever among natives of warm countries less is known. Castellani (2) states that it is common. He says: "In most cases the temperature does not run the typical course described in text books on general medicine, having sometimes a high remittent type, and at others an intermittent type, while cases of mixed infection with malaria are not rare." Rogers (3) found typhoid to be common among natives in India and believes it would be more frequently observed were it not that adult natives have acquired an immunity as a result of an attack in childhood. The sick native children are not often seen by competent attendants.

#### REPUTED OCCURRENCE OF TYPHOID FEVER IN THE PHILIPPINES.

In the early days of the American occupation of the Philippines it was the commonly accepted view that the occurrence of typhoid in these Islands was unusual.<sup>(10)</sup> That this opinion still has adherents is shown by the statements published in 1910 by Dr. Victor G. Heiser, Director of Health of the Philippine Islands. He says: "While cases

of typhoid fever are undoubtedly contracted in the Philippines the disease can hardly be said to be prevalent here. To prevent its acquiring a foothold regulations were prepared \* \* \*"(9)

For a number of years, especially since more settled conditions have allowed general resort to laboratory methods, the belief has been growing among medical officers of the army that typhoid fever is by no means infrequent in the Archipelago. It is our opinion that the disease is wide spread and very common in the Philippine Islands among both white men and natives.

Nichols in 1908 called attention to the frequent occurrence of typhoid fever among the Filipinos in the Visayas especially among the children.(11) Bruns, about the same time, stated that in his opinion typhoid was endemic in Iloilo.(12) Nichols also found typhoid fever among the natives at Taytay, a typical Tagalog town located about 32 kilometers from Manila.(13) La Garde(15) and Jackson(10) have both expressed the opinion that the frequency of typhoid among the natives is not sufficiently appreciated. Brownlee, formerly stationed at Malabang in Mindanao, states that he has found typhoid quite prevalent in Mindanao.(4) Dulin, after a long tour of duty in the Cotabato Valley, reached the conclusion that typhoid is endemic at all times and in all places in that portion of Mindanao.(4) Shockley, who has seen much service in Mindanao, confirms the above opinions as to the prevalence of the disease in that island.(4) Arlington Pond in a personal letter gives it as his opinion that there is much more typhoid in the Island of Cebu than is recognized. W. A. Powell from Lucena mentions the occurrence of typhoid among both adults and children. Huber states that he finds typhoid almost constantly present in the town of Bayambang, Pangasinan Province, Luzon.(14) Phalen, for two years president of this Board, voiced the belief that typhoid is an ever present endemic disease throughout the Philippines.(4) Many other medical officers of the army have verbally expressed the same opinion. Spanish and Filipino practitioners refer to the frequent occurrence of a "calentura", a fever of two or three weeks' duration which does not yield to quinine.

As will appear later, our laboratory findings confirm the above opinions as to the *wide range* of typhoid infection in the Philippines but can not, of course, throw much light on the *frequency* of its occurrence in the native population.

TYPHOID STATISTICS FOR THE PHILIPPINES FURNISHED BY THE BUREAU OF HEALTH.

Vital statistics in the Philippines, particularly outside Manila, are notably unreliable because of the scarcity of competent physicians and because of the great number of natives who are never seen by any medical attendant even in an illness terminating fatally. In view of the almost universal tendency to ignore typhoid fever and to consider malaria the cause of the doubtful fevers it is probable that the following figures, obtained from the Bureau of Health, do not err in the direction of exaggerating the death rate from enteric fever.

TABLE I.—Typhoid fever in the Philippines.

Calendar year.	Number of deaths.	
	Manila. <sup>a</sup>	Provinces. <sup>a</sup>
1906.....	47	2,453
1907.....	77	2,133
1908.....	116	2,371
1909.....	90	2,387
1910.....	82	
Average.....	82.4	2,336

<sup>a</sup> The population of Manila in 1907 was 223,543, divided as follows: Americans and Europeans 9,079; Chinese 18,028; Filipinos 195,292; others 1,143. The population of the provinces referred to is approximately 6,434,390.

Granting a death rate of 20 per cent (which seems a liberal one and is much higher than the experience of the army among either white or native soldiers), the average of 82.4 deaths annually would indicate a yearly incidence of 412 cases of enteric fever in Manila or one *per* year for each 542 persons.

This average yearly rate of 82.4 deaths in a city of 223,543 people represents a mortality of 36.8 per 100,000. The Census bulletins for the registration areas in the United States show the death rate from typhoid per 100,000 to have been 25.3 for 1908, 30.3 for 1907, and 32.2 for the period 1901 to 1905.<sup>(22)</sup> The rate per 100,000 from 1901 to 1905 averaged 11.4 for Scotland, 11.2 for England and Wales, 13.1 for Ireland, 16.8 for Belgium, and 7.6 for Germany.

The following list shows the position of Manila as compared with certain large cities in Europe<sup>(23)</sup> and America.<sup>(22)</sup>

[The figures indicate deaths from typhoid per 100,000 of population.]

City.	Deaths.	City.	Deaths.	City.	Deaths.
1. Pittsburgh.....	129.6	8. MANILA.....	36.8	15. Omaha.....	20.3
2. Allegheny.....	110.1	9. Toledo.....	36.3	16. Milwaukee.....	18.1
3. Washington.....	56.6	10. Baltimore.....	35.8	17. New York.....	18.1
4. Philadelphia.....	52.3	11. Buffalo.....	28.9	18. London.....	12.3
5. New Orleans.....	40.9	12. Chicago.....	28.4	19. Hamburg.....	5.6
6. Memphis.....	37.8	13. San Francisco.....	27.0	20. Vienna.....	4.3
7. St. Louis.....	37.2	14. Boston.....	22.2	21. Berlin.....	3.8

As compared with American communities it will be seen that Manila corresponds with the middle group including such places as New Orleans, St. Louis, Toledo, and Baltimore. It is exceeded only by a few cities which are notorious for high typhoid rates. Its mortality record is far above that for the best American cities which themselves have an enor-

mously greater typhoid rate than do many of the municipalities of Europe.

As regards the accuracy of the typhoid death rate in Manila, Doctor Andrews, in charge of the city morgue, states that he encounters many cases of typhoid at the autopsy of native bodies and that he considers the average of 82 deaths per year to be well within the limits. Most of the cases he finds have been undiagnosed or incorrectly diagnosed.

THE INCIDENCE OF TYPHOID AMONG AMERICAN SOLDIERS IN THE PHILIPPINES.

Considerable doubt may attach to the accuracy of the diagnoses in some of the deaths reported to the Bureau of Health as caused by typhoid, but in the case of the Army statistics for Americans during the past ten years this possibility of error is reduced to a minimum, since every soldier seriously ill is treated in hospital and the diagnosis in nearly all instances is made with the aid of laboratory facilities.

During the year 1898 typhoid was everywhere epidemic among the untrained volunteer troops in the United States. Throughout 1899 it decreased at the home stations but was widely prevalent in the Philippines among the great numbers of newly recruited volunteers who were undergoing the hardships of a strenuous campaign. These two years would show nothing of value when comparing the admission rates for troops serving in the Philippines and in the United States. Therefore, they have been omitted from the tables below which begin with the year 1900 and are compiled from the reports of the Surgeon General of the Army.

TABLE II.—Typhoid fever in the United States Army, American troops.

Calendar year.	Philippine Islands.					United States.				
	Mean strength.	Admissions.		Deaths.		Mean strength.	Admissions.		Deaths.	
		Num-ber.	Per 1,000.	Num-ber.	Per 1,000.		Num-ber.	Per 1,000.	Num-ber.	Per 1,000.
1900_____	66,882	716	10.71	141	2.11	20,690	115	5.56	9	0.43
1901(16)_____	59,526	315	5.29	58	0.97	26,115	250	9.43	17	0.64
1902(17)_____	32,942	201	6.10	32	0.97	39,736	341	8.58	34	0.86
1903(18)_____	18,671	82	4.39	15	0.80	42,264	246	5.82	12	0.28
1904_____	11,996	23	1.92	5	0.42	43,940	247	5.62	12	0.27
1905_____	11,057	31	2.80	3	0.27	42,834	153	3.57	13	0.30
1906_____	12,380	48	3.88	0	0.00	40,621	230	5.66	11	0.28
1907_____	11,699	41	3.50	3	0.26	35,132	124	3.53	7	0.19
1908_____	11,971	33	2.76	5	0.41	46,316	136	2.94	11	0.23
1909_____	12,844	79	6.15	2	0.15	57,124	173	3.03	16	0.28
Total_____	249,968	1,569		264		394,772	2,015		141	
Average for 10 years_____	24,997	156.9	<sup>a</sup> 6.28	26.4	<sup>a</sup> 1.06	39,477	201.5	<sup>a</sup> 5.10	14.1	<sup>a</sup> 0.36

<sup>a</sup> Average admissions and deaths per 1,000 are based on the average of admissions and deaths for ten years as compared with average mean strength for same period.

For comparison with the above there is given below a table covering the same period and showing the number of admissions for malarial fevers and fevers of undetermined causation.

TABLE III.—*Malaria and undetermined fevers in the United States Army, American troops.*

Calendar year.	Philippine Islands.				United States.			
	Mean strength	Fevers undetermined, admissions per 1,000.	Malarial fevers.		Mean strength	Fevers undetermined, admissions per 1,000.	Malarial fevers.	
			Admissions per 1,000.	Deaths per 1,000.			Admissions per 1,000.	Deaths per 1,000.
1900.....	66,882	29.01	874.28	1.59	20,690	9.67	158.47	0.19
1901.....	59,526	25.38	501.62	0.65	26,515	8.22	109.07	0.00
1902.....	32,942	20.23	462.94	0.64	39,736	7.65	93.09	0.06
1903.....	18,671	(*)	451.33	1.26	42,264	(*)	57.46	0.00
1904.....	11,996	33.34	218.32	0.25	43,940	6.25	47.43	0.00
1905.....	11,057	35.27	258.84	0.54	42,834	6.91	43.84	0.02
1906.....	12,380	8.97	304.20	0.55	40,621	7.73	50.27	0.02
1907.....	11,699	15.73	167.79	0.17	35,132	4.67	30.20	0.00
1908.....	11,971	25.31	123.97	0.16	46,316	3.80	26.69	0.00
1909.....	12,844	25.46	112.35	0.15	57,124	2.15	23.06	0.00

\* No data.

There was no mortality for the undetermined fevers shown in the Table III except in 1900 when it was 0.01 per 1,000 in the Philippines and 0.05 per 1,000 in the United States.

On studying these tables it will be observed that for the ten-year period the typhoid admission rate per 1,000 has been higher in the Philippines than in the United States, 6.28 as compared with 5.10. The death rate from typhoid has been three times as high in the Philippines, 1.06 per 1,000 as compared with 0.36. During the years 1907 and 1908, when the sanitary conditions and the service conditions in the Philippines closely approximated those at home, the typhoid admission rate has not materially differed in the two countries while in 1909 it was twice as high in the Philippines as in the United States. The admissions for 1910 have been 38, making an admission rate of approximately 3.1 per 1,000 which exceeds the home rate for 1908 and 1909.

In considering the comparative admission rates for typhoid in the Islands and at home, it is important to bear in mind that in the United States the water supplies of many towns and posts are not above suspicion, yet little care is generally exercised by soldiers to avoid drinking these doubtful waters. In the Philippines distilled water of unquestioned purity is everywhere furnished for soldiers and the fear of dysentery and cholera, together with the stringent orders on the subject, make the drinking of this water very general. If the same carelessness in drinking which we see everywhere at home were practiced here, we believe that the typhoid rate would be very much higher than it is at present.

A consideration of the above remarks points very strongly to a wide spread and easily accessible source of typhoid infection in these Islands.



That this source is also accessible to the native troops is shown by the following table:

TABLE IV.—*Admissions among Philippine (Native) Scouts of the United States Army for typhoid, malaria, and undetermined fevers.*

Calendar year.	Mean strength	Admissions.				Deaths. <sup>a</sup>		
		Typhoid fever.		Malaria fever per 1,000.	Fever, undetermined, per 1,000.	Typhoid fever.		Malaria fever per 1,000.
		Num-ber.	Per 1,000.			Num-ber.	Per 1,000.	
1902.....	4,826	9	1.86	704.11	35.02	1	0.21	1.66
1903.....	4,888	5	1.02	522.09	0.00	1	0.20	2.45
1904.....	4,610	4	0.87	367.69	34.49	3	0.65	0.43
1905.....	4,732	7	1.48	571.01	15.64	2	0.40	0.81
1906.....	4,759	4	0.84	393.15	21.43	1	0.20	1.19
1907.....	4,679	6	1.28	312.67	19.45	0	0.00	0.43
1908.....	5,085	9	1.77	236.97	20.45	0	0.00	0.19
1909.....	5,369	7	1.30	203.95	17.69	1	0.18	0.00
Total.....	38,948	51				9		
Average for 8 years.....	4,619	6.38	1.36			1.13	0.24	

<sup>a</sup> There were no deaths from undetermined fevers.

Table IV shows that there has been a constant, though low, admission rate for typhoid among the Philippine Scouts since their organization. It is certain that the diagnoses for sick Scouts are less thoroughly worked up than are those of the white troops because of racial peculiarities and the difficulty of understanding their language, and also because of the fact that many of the Scout organizations are at small and isolated posts with meager laboratory facilities. Therefore, some cases of typhoid may lie hidden in the great mass of admissions for malaria and undetermined fevers, only the most characteristic cases being correctly diagnosed.

Since most of the Scouts are at posts where they come in contact with very few white men, it is almost certain that they pick up their infection at the post or in the country surrounding and that the disease is not imported from the United States as might be urged in the case of the white soldiers.

The lesser incidence of typhoid among the Scouts as compared with American troops corresponds with Rogers' experience with native troops in India. He attributes this difference to the influence of typhoid in childhood.

#### DISTRIBUTION OF TYPHOID FEVER IN THE PHILIPPINES.

The distribution of typhoid throughout the Archipelago, in so far as it has come under the notice of the Army medical officers, is shown in Table V.

TABLE V.—*Distribution of typhoid fever in the Philippines, Army statistics.*

Town or post.	Island.	Number of admissions for typhoid fever.									Total.
		1904	1905	1906	1907	1908	1909	1910	1911 part.		
Keithley	Mindanao		2	11	+	1				15	
Marahui	do	5								5	
Cotabato	do		(1)			(1)		2 (1)		2 (3)	
Vicars	do	3								3	
Overton	do						1	1	1	3	
Malabang	do	2		1	+		4		1	9	
Ludlow	do										
Parang	do	1					51 (2)	22 (4)	(2)	73 (8)	
Polloc	do						(5)			1 (5)	
Field	do			3					(2)	(2)	
Zamboanga	do	1	1	2	+		1			4	
Jolo	Jolo						1			5	
Balamban	Cebu					(1)				1	
Cebu	do								(1)	(1)	
Naga	do						1			1	
Field	do		1							1	
Downes	Leyte						3	1	1	5	
Dagami	do				(2)					(2)	
Field	do			1	13					14	
Bumpus	do						11			11	
Connell	Samar			2	+					6	
Balangiga	do		3		(1)					(1)	
Field	do		1							1	
	Negros										
					1					1	
Jossman	Guimaras	1	1	1	+					6	
Iloilo	Panay				3			1	1	3	
San Pedro	do			15	8	2				25	

Mills	Corregidor					2 (1)	2	1 (1)	5 (2)
Stotsenburg	Luzon		1	3	3	1	2	1	11
Lucena	do						(3)		(3)
Gregg	do		7	+			(13)		8 (13)
Infanta	do			(1)					(1)
Wallace	do	3	1	+			(1)		5 (1)
San Fernando, Union	do						(19)		(19)
Pasay	do	1							1
Wilhelm	do							(1)	2 (2)
Manila Posts *	do	3	8	7	12 (1)	2 (1)	12 (3)	2 (2)	46 (7)
Imus	do					1			1
Daraga	do	2	2	+					5
Floridablanca	do							2	2
Bakoor	do	1							1
Los Baños	do					1			1
Bulan	do	1							1
Eldridge	do					10			10
McGrath	do	1				1	1	1 (1)	4 (1)
Bayambang	do						(2)		(2)
Cañacao	do							(1)	(1)
Pilar	do	1							1
Mariveles	do					1			1
McKinley	do		8	1	2	2	2	1	20
Field	do		2						2
San Pablo	do							(1)	(1)
Malahi	do		1						1
Total		23	31 (1)	48	37 (4)	81 (9)	48 (47)	10 (12)	323 (76)

<sup>a</sup> Includes Division Hospital.

Numbers inclosed in parentheses ( ) represent native cases. No statistics available for natives 1904-1906.

Numbers entered in parentheses ( ) represent minor cases. Spaces marked with a plus sign (+) indicate that one or more cases occurred at the locality indicated but the records do not show the number at many of the posts and give only the total for the year. In the horizontal totals the item marked with a plus sign (+) has been counted as one case only, consequently horizontal and vertical grand totals do not agree.

The figures in Table V were obtained from the reports of the Surgeon General of the Army, the records of the chief surgeon, Philippines Division, the records of this Board, and in a few instances from personal knowledge of members of the Board. The table does not pretend to be complete but it is sufficient to indicate how widely spread throughout the Archipelago is the infection with typhoid. The accompanying "spot map" graphically indicates the distribution. In considering Table V it must be borne in mind that the localities mentioned represent a majority of the places in the Islands where there are competent observers or laboratory facilities.

The Bureau of Health mortality statistics for the provinces cover all parts of the Archipelago except Mindanao, Jolo, and adjacent small islands. These reports show typhoid to be an extremely common cause of death in all of the important islands, the mortality rate in some provinces for certain years ranging from 50 to more than 160 per 100,000 of population. We have not gone into these figures in more detail because of the uncertainty which attaches to the diagnosis of typhoid, or any other disease for that matter, in the provincial reports.

WIDAL EXAMINATIONS ON THE BLOOD OF HEALTHY ADULT NATIVES.

With a view to determining how large a proportion of healthy natives might show the influence of antecedent typhoid, as evidenced by a positive Widal reaction, the Board has obtained the blood of 307 adult male Filipinos and the results are shown in Table VI. These examinations were made in 1910 and 1911.

TABLE VI.—Widal examinations on the blood of healthy Filipino adults.

Station or town.	Island.	Race or tribe.	Number.	Widal, dilutions about 1 to 20.		Widal, dilutions about 1 to 50.	
				Positive.	Negative.	Positive.	Negative.
Parang .....	Mindanao .....	Moro .....	12	1	11	1	0
Parang .....	do .....	Filipino .....	52	4	48	4	0
Camp Wilhelm .....	Leyte .....	Visayan .....	12	0	12		
Camp James .....	do .....	do .....	12	0	12		
Cotabato .....	Mindanao .....	Ilocano .....	12	0	12		
Camp Wallace .....	Luzon .....	Visayan .....	12	0	12		
Regan Barracks .....	do .....	Ilocano .....	12	2	10	0	2
Camp Connell .....	Samar .....	Visayan .....	12	2	10	0	2
Isabela .....	Basilan .....	Moro .....	12	0	12		
Bojelebung .....	do .....	do .....	6	0	6		
Bumpus .....	Leyte .....	Visayan .....	12	1	11	0	1
Fort Mills .....	Corregidor .....	Macabebe .....	36	4	32	2	2
Camp Gregg .....	Luzon .....	Visayan .....	40	0	40		
Camp Hay .....	do .....	Igorot .....	20	2	18	0	2
Camp Hayt .....	Samar .....	Cagayan .....	12	4	8	2	2
Kaligton .....	Luzon .....	Ilocano .....	13	0	13		
Fort Mills .....	Corregidor .....	Visayan .....	20	0	20		
Total .....			307	20	287	9	11
Percentage .....				6.5	93.5	2.9	

Reactions in 1 to 50 dilution were done only on those cases which proved positive in 1 to 20 dilution.

There are few data available to indicate what proportion of healthy men in any country might give a positive serum reaction from causes other than antecedent typhoid. The length of time that the Widal reaction persists after convalescence from enteric fever is variable, ranging from six weeks to twenty years, the long continuance in some cases perhaps being due to bacilli persisting in the gall bladder. The fact that 6.5 per cent of the adults we tested showed a positive reaction in 1 to 20 dilution and 2.9 per cent in 1 to 50 dilution probably points to an antecedent attack of typhoid in some of these individuals and, when taken with the statistical evidence already presented, is suggestive of a wide spread distribution of the disease in the native population.

THE INFREQUENCY OF SEVERE AND FATAL EPIDEMICS AMONG NATIVES.

The above quoted statistics and examinations indicate to our minds that typhoid is very generally present in the Philippines. The water supplies are almost universally bad, the proper disposal of excreta is almost entirely neglected, the crowding in the habitations and the native manner of eating favor contact infection. Yet, in spite of these unfavorable conditions, there is little evidence that severe and destructive epidemics of typhoid fever occur among the Filipinos. The relative scarcity of typhoid among the natives in India is thought by Rogers to be due to immunity acquired in childhood. Nichols<sup>(11)</sup> expresses the opinion that typhoid is prevalent among children in the Philippines. To determine if evidences of previous typhoid in Filipino children could be detected, we performed Widal reactions on the blood of 284 healthy school children. The results are shown in Table VII and are entirely negative except for three cases at Ormoc, a town where we had good reason to believe that typhoid had recently prevailed.

TABLE VII.—*Widal examinations on the blood of healthy Filipino school children.*

Town.	Island.	Race or tribe.	Number.	Widal, dilutions about 1 to 20.		Widal, dilutions about 1 to 50.	
				Positive.	Negative.	Positive.	Negative.
Baguio	Luzon	Igorot	45	0	45		
Paranaque	do	Tagalog	30	0	30		
Lucena	do	do	50	0	50		
Ormoc	Leyte	Visayan	14	3	11	1	2
Malabang	Mindanao	Filipino	7	0	7		
Parang	do	do	30	0	30		
Iligan	do	do	22	0	22		
Jolo	Jolo	Moro	36	0	36		
Floridablanca	Luzon	Filipino	26	0	26		
San Nicolas	do	do	24	0	24		
Total			284	3	281	1	2
Percentage				1.0	99.0	0.3	

It will be seen that the percentage of positive results was much less than among adults. These children ranged from four to thirteen years of age and the majority were under eight years old. If typhoid were common among the Filipino school children, it is probable that the percentage of positive reactions among them would be considerable. It is possible, of course, that the disease may occur widely among infants and that the agglutinating influence in nearly all cases had passed away before the time at which we saw these children. However, such an explanation does not appear to us probable.

Our clinical records, to be discussed later, indicate that a considerable number of the cases which give positive laboratory finding present clinical appearances entirely different from the classic description of typhoid fever. Patients with a short course, little fever and few symptoms, were found commonly among both Americans and Filipinos. It is by no means unlikely that such cases throughout the native population are very common and that the true nature of the malady is overlooked. The disease in this form can be diagnosed by laboratory procedures alone, and it is only by working along this line that the true incidence of typhoid fever among the Filipinos can be determined.

#### INFLUENCE OF SEASON ON PREVALENCE OF TYPHOID.

In Europe and America typhoid fever may occur at any season, but its incidence is greatly increased in August, September, and October. In India, as a whole, Roberts has shown that the disease is very generally distributed throughout the year as follows: first quarter 18.1 per cent; second quarter 31.3 per cent; third quarter 28.1 per cent; fourth quarter 22.4 per cent. The experience for four years (the only ones for which monthly records are available to us) shows that in the Philippines the disease is distributed throughout the year in a quite regular manner.

TABLE VIII.—*Incidence of typhoid fever by months in the Philippines.*

Month.	1904.	1908	1909	1910	Total.	Quarter.	
						Number.	Per cent.
January -----	2	3	1	7	13	78	24.61
February -----	1	5	7	10	23		
March -----	1	13	7	21	42		
April -----	1	8	1	2	12	44	13.88
May -----	0	9	2	0	11		
June -----	5	14	2	0	21		
July -----	4	25	5	4	38	90	23.39
August -----	2	23	8	0	33		
September -----	1	14	3	1	19		
October -----	3	12	43	2	60	105	33.12
November -----	1	17	3	0	21		
December -----	2	13	5	4	24		
Total -----	23	156	87	51	317		

The considerable increase in the last quarter may be considered accidental since the 43 cases in October, 1909, all occurred at one post, the Ludlow Barracks epidemic.

The season varies considerably in the Philippines in different localities and for different years, but in general it may be said that the period from December 1 to June 1 represents the dry season.

Since our military patients mainly are drawn from a population consisting almost exclusively of young adult males, it has been impossible for the Board to draw any conclusions as to the influence of sex or age on the incidence of typhoid in the Philippines except in so far as we have mentioned the latter factor in the paragraph below Table VII.

#### PART II. LABORATORY INVESTIGATIONS OF TYPHOID FEVER IN THE PHILIPPINES.

During the two and one-half years that the Board has been working on the subject of typhoid fever the following examinations have been made in the case of persons having typhoid fever or suspected of having it.

TABLE IX.—*Examinations by the Board on persons suspected of having typhoid, December 1, 1908 to April 30, 1910.*

Results.	Widal tests.	Cultures from—			
		Stools.	Urines.	Blood.	Bile.
Positive .....	192	19	9	17	1
Negative .....	261	498	320	139	0
Total .....	453	517	329	156	1

The 453 serum reactions were performed on the blood of 369 persons. The 192 positive Widal reactions were made on the blood of 177 persons, of whom 118 were Americans and 59 were Filipinos. The 517 stool cultures were made on 199 individuals, the 329 urine cultures on 164 individuals, and the 156 blood cultures on 141 individuals.

#### BLOOD CULTURES, 17 POSITIVE, 139 NEGATIVE.

The organisms were sought in the blood by placing it in sterile bile, incubating for twenty-four hours and plating on Endo medium. Many of our specimens of blood were very old and the amount small, which accounts partially for the small number of positive findings. The fact that the disease in many instances was far advanced needs also to be considered. All of our positive blood cultures were obtained from patients in the Division Hospital or at posts we visited, and from these patients we obtained a large amount of blood and placed it at once in the bile medium. Since all of these cases came under our immediate observation, we feel sure that the days of the disease, as shown in the following table, are approximately correct.

TABLE X.—*Days on which positive blood culture was obtained.*

Day.	Number positive.	Day.	Number positive.
Second .....	1	Twelfth .....	1
Third .....	1	Thirteenth .....	1
Sixth .....	2	Fourteenth .....	1
Seventh .....	2	Unknown .....	1
Eighth .....	3	Total .....	17
Ninth .....	3		
Eleventh .....	1		

Among the cases which showed bacilli in the blood at the end of the first week or later the following are of interest:

TABLE XI.—*Relation of Widal reaction to positive blood culture.*

Case.	Day.		
	Blood positive.	Widal negative.	Widal positive.
3	Fourteenth .....	Twelfth .....	Fourteenth.
4	Seventh .....	Seventh .....	Ninth.
258	Eighth .....	Sixth .....	Ninth.
W.	Seventh .....	Sixth and tenth .....	Twenty-first.
B.	Eighth .....	Seventh .....	Eighth.
T.	Twelfth .....	Twelfth .....	(?)
402	Sixth .....	Sixth and seventh .....	Twenty-second.

STOOL CULTURES, 19 POSITIVE, 498 NEGATIVE, AND URINE CULTURES, 9 POSITIVE, 329 NEGATIVE.

Stool and urine specimens were smeared over the surface of Petri dishes containing Endo medium. Cultures from the excreta were rarely employed for diagnosis. Nearly all of those shown in the table were made during convalescence to detect possible carriers, three negative cultures at six-day intervals being required before a soldier was returned to duty. These facts account in the main for the low proportion of positive findings. Another factor which must be considered is that the stools and urines in many cases had come a long distance. Our experience, both practical and experimental, has been that after a few days no typhoid bacilli can be obtained by cultural methods from a stool, whether naturally or artificially inoculated with *Bacillus typhosus*.

#### CHARACTER OF TYPHOID ORGANISM ISOLATED IN THE PHILIPPINES.

At the end of 1908 this Board had found the blue strain of typhoid in 5 patients in the Philippines and expressed the opinion that the prevailing type of organism in the Philippine Islands might be one which produced primary acidity in litmus milk followed after several days by alkalinity. Further experience has not confirmed this view. During nearly two years we have isolated only one blue typhoid organism from either a native or a white man, and



recently, on re-testing a number of organisms isolated in the Philippines, all except that one failed to give the blue reaction. Therefore, it is, probable that the blue strain occurs with no greater degree of frequency in the Philippine Islands than in the United States. The distinction in type is probably of no importance and the variations reported may at times be due to the use of milks containing variable quantities of monosaccharid. In fact, acidity followed by alkalinity is given as the type for typhoid by Hiss and Zinsser.<sup>(20)</sup>

It appears that there is no constant difference, either in their litmus-milk reaction or in their behavior in the presence of immune sera, between the strains of *Bacillus typhosus* found here and those met with in the United States.

WIDAL EXAMINATIONS, 192 POSITIVE, 261 NEGATIVE.

The 192 positive examinations were made on the blood of 177 individuals of whom 5 had received antityphoid vaccination and two others gave a clear history of previous typhoid, leaving 170 cases in which the positive reaction was of diagnostic value.

Only the microscopic method was employed by us in making the agglutination test, both loss of motility and clumping being required before making a positive report. A dilution of 1 to 50 was used and one hour allowed to elapse before recording the result. Part of these tests were made with fluid blood and the remainder with dried blood, the dilution in the latter cases being, of course, only approximate.

Nichols<sup>(11)</sup> and Bruns<sup>(12)</sup> in the Islands of Leyte and Panay investigated two epidemics in which they found an absence of the Widal reaction until very late in the disease. In 11 cases Nichols found it absent on an average till the twenty-fifth day. In the 177 positive Widal reactions obtained by us we were often dependent on others for the statement of the day of the disease. As thus given, the figures are as follows:

TABLE XII.—Days on which positive Widal reactions were obtained.

Day.	Num- ber.	Day.	Num- ber.	Day.	Num- ber.	Day.	Num- ber.
Second .....	13	Eleventh .....	7	Twentieth .....	1	Forty-fifth .....	1
Third .....	13	Twelfth .....	1	Twenty-first .....	3	Fifty-eighth .....	1
Fourth .....	12	Thirteenth .....	5	Twenty-third .....	1	Seventy-third .....	1
Fifth .....	14	Fourteenth .....	3	Twenty-fifth .....	1	Unknown <sup>a</sup> .....	35
Sixth .....	8	Fifteenth .....	2	Twenty-sixth .....	3	Total .....	177
Seventh .....	14	Sixteenth .....	2	Twenty-seventh .....	1		
Eighth .....	12	Seventeenth .....	1	Thirtieth .....	2		
Ninth .....	6	Eighteenth .....	3	Thirty-sixth .....	1		
Tenth .....	5	Nineteenth .....	3	Thirty-seventh .....	2		

<sup>a</sup> This "unknown" group contains 5 positive Widal's obtained in persons who had been vaccinated against typhoid and who did not have the disease, 2 obtained in persons not suffering from typhoid but giving a clear history of a previous attack, a few from whom we never received records, and a series of 20 natives found at San Fernando who undoubtedly had the disease but from whom no history was obtainable.

From a study of the temperature charts of the patients we feel sure that many of the cases were somewhat further along in the disease at the time of the appearance of the Widal reaction than would be indicated by the above figures. On the other hand, most of the cases reported above as having a very late serum reaction undoubtedly would have shown one earlier, but none was done till the date indicated in the table. In a series of cases in which a negative followed by a positive reaction was obtained and in which the onset of the disease has been fixed with reasonable accuracy from the clinical records we found no notable prolongation of the pre-agglutination stage. The figures appear in Table XIII.

TABLE XIII.—*Days on which Widal appeared in patients who had previously given a negative reaction.*

Case number.	Day.		Case number.	Day.	
	Widal negative.	Widal positive.		Widal negative.	Widal positive.
5	Sixth and seventh	Eighth.	117	Seventh and eighth	Tenth.
21	Tenth	Eleventh.	108	First and third	Fourth.
7	Seventh	Eighth.	138	Sixth	Seventh.
4	Seventh	Ninth.	131	Second	Fourth.
3	Twelfth	Thirteenth.	128	Second	Fifth.
258	Sixth	Ninth.		Seventh	Eighth.
1076	Sixth	Seventh.	213	Fifth	Tenth.
350	Second	Fourth.	402	Sixth and seventh	Twelfth.
352	Seventh	Eighth.		Average	Ninth.
383	Fifteenth	Twenty-fourth.			
137	Fourth and seventh	Tenth.			

From our 89 characteristic cases of typhoid fever, analyzed below and in which the date of onset could be quite definitely fixed, we obtained positive Widal reactions on or before the tenth day of the disease in 72 per cent and on or before the fifteenth day in 87 per cent. In all but one of the remaining 13 per cent no serum test had been performed prior to the fifteenth day, and it is probable that all or nearly all were positive before that time.

From the above figures it is evident that the experience of the Board *does not indicate any general tendency toward unusual delay in the development of agglutinins in the blood of patients suffering from typhoid fever in the Philippines.*

We have analyzed the clinical records of over 100 patients with elevations of temperature and for whom negative Widal reactions were obtained. In only one instance was there the slightest reason to believe that the febrile condition was enteric fever, and in this single case the temperature curve and symptoms were not entirely characteristic. Repeated typhoid serum reactions were negative up to the fourteenth day, after which time no specimens were submitted. Serum reaction with *Bacillus paratyphosus* was reported negative but fell in the class of reactions which some observers report as "partial." The leucocyte count was 9,000 and there was 33.8 per cent of small lymphocytes and 9.2 per cent large

mononuclears. No pigmented leucocytes were seen. A relapse occurred in this patient which promptly yielded to hypodermic use of quinine although previous examinations for parasites and previous use of quinine by mouth had resulted negatively. The true nature of this case remains in doubt.

#### TYPHOID BACILLUS CARRIERS.

Failure attended our efforts to detect carriers as a result of 517 stools cultures made on 199 individuals and 329 urine cultures made on 164 individuals. However, we discovered one typhoid bacillus carrier by accident while examining for dysentery the stool of a patient who had been having loose movements of variable frequency for nearly 4 months.

The patient, aged 30, gave no history of typhoid fever. He had been in the Philippines one year and had ten years' service in the Army. He had dysentery in 1907. The last part of June, 1910, while on a mapping detail in the field, he developed a very severe attack of diarrhœa with some blood and mucus. Did not go on sick report and diarrhœa persisted. Lost about 28 pounds in weight. On admission to Division Hospital September 5, 1910, he was having about 4 stools daily, usually liquid and yellowish or clay-colored. They contained neither blood nor mucus. During his stay in the hospital from September 5 to October 14, 1910, his temperature never went above 37°.4C. and was generally normal. Pulse averaged 90 at times reaching 110. Repeated examinations of the stools for ova and amœbæ were negative.

The first stool culture was made on October 13, the day before he sailed for the United States and about 110 days after his original attack of diarrhœa. It was positive for *Bacillus typhosus*. Meantime the patient had sailed for the United States, but by telegraphic request we obtained a specimen of his blood while the transport was at Mariveles and this gave a positive Widal reaction.

Under date of November 19, 1910, the commanding officer of the General Hospital at Presidio of San Francisco notified us that the soldier was still excreting typhoid bacilli.

As far as we can learn this is the only carrier which has been found in the Philippines.

#### PARATYPHOID FEVER AND GROUP AGGLUTINATION.

Strong in 1902 reported the recovery at autopsy of a paracolony organism from a soldier who had died with the usual symptoms of typhoid.<sup>(21)</sup> Ruediger, at the Bureau of Science, recently isolated a para-typhoid strain from the blood of a dog which died of rabies and showed also a purulent pneumonia. Our experience with the paratyphoid organism is confined to one case. The patient, who also had tuberculosis, ran a febrile course of eighteen days' duration, the curve suggesting mild typhoid fever. There were the usual premonitory symptoms of typhoid fever, and the progress of the disease was characterized by constipation, tympanites, pain in head and neck, splenic tumor, and normal leucocyte count. From the blood was obtained a pure culture of *Bacillus paratyphosus* "A." The blood serum at first agglutinated both *Bacillus typhosus* and *Bacillus paratyphosus*. At a later date it failed to react with the former organism.<sup>2</sup>

<sup>2</sup> Since this writing we have isolated *Bacillus paratyphosus* "A" from the blood of a Japanese with a continued fever at Camp Stotsenburg.

We have tried the agglutination reaction with *Bacillus paratyphosus* on a considerable number of patients, and aside from the above have obtained positive reactions only twice, one of these sera also reacting with *Bacillus typhosus*. A more detailed report of the above case and a discussion of the subject of group agglutinations is contained in our quarterly report for December 31, 1910.

#### OBSERVATIONS ON THE BLOOD OF TYPHOID FEVER PATIENTS.

The blood of all of the patients considered was examined for malarial organisms with negative results except as noted below under complications. No other blood work was done on the cases except leucocyte counts, most of which were made at the laboratory of the Division Hospital on patients who were being treated in that institution. Thirty-six white blood counts were made on the blood of 19 patients and 31 differential counts on 15 of the same individuals. The average results divided as to race, appear below:

TABLE XIV.—Average white blood counts on typhoid fever patients.

Average.	Leucocytes per c. mm.	Polymorphonuclears.	Small lymphocytes.	Large lymphocytes.	Transitionals.	Eosinophiles.	Mast cells.
Americans -----	6,540	66.2	25.7	6.3	1	0.6	0.1
Filipinos -----	10,234	66.9	26.3	5.3	0.3	0.5	0.7
Both races -----	7,669	66.5	25.9	6	0.8	0.6	0.3

These counts were made in the first week or ten days of the disease and do not show a tendency to the usual leucopenia, the average being normal for the white men and rather above normal for the natives. The lowest count for a native was 6,300 and the highest 15,400. For the Americans ten counts were below 6,000, fourteen between 6,000 and 10,000, and one was 11,500.

Rogers in a study of typhoid in India found the small lymphocytes to be increased above the normal maximum of 30 per cent in over one-half his patients. In our series this was not the case, in fact we should consider the average of 25.9 per cent as low, since it has been our experience that in the Philippines the count of the small lymphocytes is uniformly high in healthy men, usually ranging above 30 per cent. This is true for natives, and for Americans with one or more years of tropical service.

The low eosinophile count in this native series is very unusual and probably is due to the fact that most of the patients were Scouts who had been relieved of their intestinal parasites prior to acquiring typhoid fever.

#### PART III. CLINICAL ASPECTS OF TYPHOID FEVER IN THE PHILIPPINES.

After excluding vaccinated patients, persons with clear histories of previous typhoid and one case of paratyphoid there remain the clinical histories of 157 patients sick during the last two and one half years and for whom the laboratory findings indicated the existence of typhoid infection. For clinical analysis we have divided these cases into four groups as follows:

Group I; 7 cases terminating fatally; 4.5 per cent.

Group II; 19 cases with short ill-defined fever of less than 10 days' duration; 12.1 per cent.

Group III; 41 cases of irregular fever of less than 10 days' duration, probably representing last part of mild ambulant typhoid types; 26.6 per cent.

Group IV; 89 cases of well marked continued fever, clinically typhoid, lasting more than 10 days; 56.6 per cent.

GROUP I. CASES TERMINATING FATALLY.

Seven patients out of the 157 died, a mortality of 4.5 per cent. The cause of death was peritonitis following perforation of the intestine in 3 instances, toxæmia in 3, and shock following hæmorrhage in one. *Bacillus typhosus* was obtained from the blood of 3 of these fatal cases and from the gall bladder of another.

Rogers found a mortality of 16.3 per cent among 129 cases in Calcutta and reports that in the British army in India the returns show a death rate of 26 to 27 per cent at the present time (1909-1910). This indicates a more serious condition than is seen in these Islands. The range in the typhoid mortality experience of the Army in the Philippines for the last ten years as contrasted with that among the troops in the United States is shown in Table XV:

TABLE XV.—*Mortality for typhoid fever in the Army in the Philippines and United States.*

Calendar year.	In the Philippine Islands.						In the United States.		
	American troops.			Filipino troops.			American troops.		
	Cases, number.	Deaths, number.	Mortality, per cent.	Cases, number.	Deaths, number.	Mortality, per cent.	Cases, number.	Deaths, number.	Mortality, per cent.
1900.....	716	141	19.69	-----	-----	-----	115	9	7.83
1901.....	315	58	18.41	-----	-----	-----	250	17	6.80
1902.....	201	32	15.92	9	1	11.11	341	34	9.97
1903.....	82	15	18.29	5	1	20.00	246	12	4.88
1904.....	23	5	21.74	4	3	75.00	247	12	4.86
1905.....	31	3	9.68	7	2	28.57	153	13	8.50
1906.....	48	0	0.00	4	1	25.00	230	11	4.78
1907.....	41	3	7.32	6	0	0.00	124	7	5.65
1908.....	33	5	15.15	9	0	0.00	136	11	8.09
1909.....	79	2	2.53	7	1	14.29	173	16	9.25
Total.....	1,569	264	-----	51	9	-----	2,015	142	-----
Average.....	-----	-----	<sup>a</sup> 16.83	-----	-----	<sup>a</sup> 17.65	-----	-----	<sup>a</sup> 7.05

<sup>a</sup> The average mortality was obtained by dividing the total number of deaths for the period under consideration by the total number of cases for the same period.

It will be observed that the average mortality is a trifle higher for the Filipino than for the American troops serving in the Philippines, 17.6 per cent as compared with 16.8 per cent. It is quite probable that

the death rate would be lower if every case of mild enteric fever occurring among the Scouts received the appropriate diagnosis. Rogers found a death rate of 26 per cent among 50 native Indian cases. Among the 26 Filipino cases for which we received clinical histories only one died, a mortality of 3.8 per cent. The average mortality for ten years among the American soldiers in the Philippines is very much higher than at home, 16.83 per cent compared with 7.05. This can be attributed mainly to the large amount of typhoid with a high mortality in the first four years of the decade, a time when the facilities for nursing, feeding and sheltering the patients were less favorable than in the United States. During the last six years, when the conditions in the Philippine hospitals have approximated those of similar institutions in the United States, the mortality has been no higher than at home (255 cases, 18 deaths, mortality 7.1 per cent). *Therefore, it seems safe to conclude that the type of typhoid infection now being encountered in the Philippines is, under present conditions, no more fatal to the American than that met with in the United States.*

GROUP II. CASES WITH ILL-DEFINED FEVER OF LESS THAN TEN DAYS DURATION.

Nineteen out of the 157 clinical records (12.1 per cent) show a slight febrile movement lasting less than ten days with few symptoms and nothing characteristic on which to base a diagnosis. The true nature of these cases could be determined only by laboratory methods. In addition to finding a clear-cut positive Widal reaction in all of the nineteen we were able to obtain by cultural methods the *Bacillus typhosus* from the stools of three and the urine of one other of this group.

GROUP III. CASES WITH IRREGULAR FEVER OF LESS THAN TEN DAYS, DURATION, PROBABLY REPRESENTING THE LAST PART OF LATENT OR AMBULANT TYPHOID TYPES.

Forty-two cases out of the 157 (26.6 per cent) presented an irregular temperature chart which resembled the last week or ten days of the classical typhoid curve. These patients were, in our opinion, suffering from a mild ambulant form of typhoid fever and came under observation only late in the disease. Such cases were particularly numerous in the Ludlow Barracks epidemic, constituting 33 per cent of the admissions, and many of them probably never would have come on sick report had it not been for the fact that the temperatures of all soldiers were being taken daily and every one with fever was placed in hospital for observation.

In addition to obtaining positive serum reactions in all of this group we isolated *Bacillus typhosus* from the stools of 5 patients and from the urine of another.

## GROUP IV. CASES WITH WELL MARKED CONTINUED FEVER LASTING MORE THAN TEN DAYS AND CLINICALLY TYPHOID.

In this group there are 89 cases (56.6 per cent of the entire 157) which ran a febrile course of ten days or more and which in nearly every instance would be considered typhoid fever from clinical observations alone. The diagnosis was confirmed in each of these cases by the laboratory findings which for the great majority were positive Widal reactions and for the remainder cultures of *Bacillus typhosus* obtained from the blood or excreta. There were 4 positive urine cultures, 5 positive stool cultures and 15 positive blood cultures from this group.

Based on clinical appearances we divided these cases as follows; typical, severe, 18 (20.2 per cent); typical, moderate, 46 (51.7 per cent); typical, mild, 10 (11.2 per cent); atypical, mild, (lacking a fastigium) 12 (13.5 per cent); atypical, severe, 3 (3.4 per cent). The clinical histories for many of these cases are deficient as regards the presence or absence of the less important symptoms and signs, therefore in the analysis which follows the percentage of occurrence for some of the minor features will be an underestimate. With all the clinical records there were well kept temperature charts which rendered easy a correct estimate of the febrile type of the disease.

*Onset of the disease.*—The onset was sudden in 4 cases and gradual in the remaining 85. The premonitory symptoms included headache, backache, pains in bones and joints, lassitude, anorexia, diarrhoea, abdominal pain, nausea, vomiting, chills, fever, stiff neck, vertigo, and myalgia. They did not differ from those commonly encountered in the United States. Chills or chilliness were recorded in 10 cases.

*Febrile course.*—The onset of the disease could be fixed with reasonable accuracy in all of these 89 cases. The lengths of the febrile reaction, collected in groups each covering a 5-day period, are shown below.

TABLE XVI.—Duration of febrile course for 89 characteristic typhoid cases.

Days.	Num-ber.	Per-cent.	Days.	Num-ber.	Per-cent.
Between 10 and 15 -----	8	8.98	Between 31 and 35 -----	9	10.11
Between 16 and 20 -----	24	26.97	Between 36 and 40 -----	10	11.24
Between 21 and 25 -----	21	23.60	Over 40 -----	4	4.49
Between 26 and 30 -----	13	14.61	Average, 25.1.		

The cessation of fever in all cases has been arbitrarily taken as the date after which the evening temperature did not rise above 37°.2 C. We believe that the above figures represent the minimum of febrile course and that possibly the real average was slightly longer as a result of the patients having been taken sick somewhat earlier than appeared upon the records. The average for our series was 25.1 days. For comparison may be mentioned the 780 cases studied by the Spanish-American

War Commission where the average duration was 10.5 days<sup>(19)</sup> and McCrae's large series in America where the average was 31 days.

The initial step-like increase of temperature characteristic of the early days in typhoid fever was rarely seen, the patients usually being well along the first week when they came under observation. A clearly marked fastigium was the rule, being present in 71 cases, 79.7 per cent of the series. For 18 persons a definite fastigium was lacking, the morning and evening excursions of temperature being pronounced even at the height of the disease. The maximum range of fever is shown below.

Never up to 39°.4 C., 9 cases. Never up to 40°.5 C., 45 cases.

Never up to 40° C., 26 cases. Never up to 41°.1 C., 9 cases.

The decline of the fever was characterized by gradually increasing remissions, such as are observed in typhoid in the United States, and no chart was found showing the unduly prolonged intermittent stage described by Rogers in India.

*Recrudescences and relapses.*—Recrudescences occurred in 4 cases (4.5 per cent) the lengths of the febrile disturbances being respectively six, seven, ten, and eleven days. Relapses occurred in 7 cases (7.9 per cent) lasting nine, twelve, fifteen, sixteen, seventeen, twenty-four, and twenty-five days, respectively. One patient was desperately ill during the relapse.

*Pulse rate.*—That the pulse rate was slow as compared with the temperature elevation was the almost universal experience, the disease in this respect conforming to the classical type in Europe and America. The low pulse rate was especially commented on by Lieutenant Dulin in the Ludlow Barracks epidemic where it rarely rose above 100 and was often normal at the height of the disease.

A dicrotic pulse was recorded in 13 out of the 89 cases, (14 per cent).

*Symptoms of intestinal origin.*—Constipation was a marked feature in this series. Diarrhœa has been credited to each patient who showed abnormal frequency for the evacuations at any time during the disease but there were only 21 such cases out of 89, an incidence of 23 per cent. Fifty-one patients (57 per cent), were constipated and, in 13 (14 per cent), the bowel movements were of normal frequency. In 4 cases there was no record. The percentage with diarrhœa is slightly higher than that found by McCrae in his American series (17 per cent) but considerably lower than that met with by Rogers in India, where 63 per cent showed diarrhœa at some period of the disease. Curschmann in Berlin found 73 per cent to have diarrhœa at some stage of the disease.

Since diarrhœa is considered of bad prognostic significance<sup>(3)</sup> <sup>(19)</sup> it may be that its low incidence among our patients is related to the low death rate of 4.5 per cent which was met with in this series.

Abdominal pain was noted as present in 13 of the 89 characteristic non-fatal cases, (14 per cent), was absent in 2 and there was no record for the remainder. Tympanites was recorded for 21 patients, (23 per



cent), was absent for 7, and for the remaining 61 there was no mention of this symptom. Vomiting at some time during the disease occurred in 13 cases, (14 per cent).

Hæmorrhage was noted in 5 instances, 5.6 per cent of the entire group. Also it was the cause of death in one of the fatal cases not included in the series of 89. This percentage corresponds closely with that found by Curschmann in Berlin and Osler in Baltimore but is much lower than the experience of Rogers who records hæmorrhage in 17 per cent of his Indian series. Perforation was seen only in the fatal cases, occurring three times.

*Symptoms referable to the nervous system.*—Headache is recorded in 40 cases, or 45 per cent. Delirium was noted for 10 patients, (11 per cent), stupor or coma for 7 (8 per cent), and subsultus tendinum in 2 (2 per cent). Under this heading may be mentioned the complications occurring in four cases, two having developed post-febrile psychosis, one a multiple neuritis of the lower extremities and the fourth a condition of cardiac and nervous irritability.

*Miscellaneous signs and symptoms.*—Rose spots were noted as present in 26 cases (29 per cent), absent in 6 (7 per cent), and in the remaining histories there is no mention. The spleen was enlarged in 18 cases (20 per cent), not enlarged in 11 (12 per cent), and in the remaining cases the records are silent on this point. Cough was present in 10 cases and bronchitis is recorded in three.

*Urine.*—Albumen was present in the urine of 13 patients (15 per cent), was absent in 19 (21 per cent). Casts were present in 8 cases (9 per cent) and absent in 19 (21 per cent). In the remaining cases there were no records of the urinary examinations.

*Complications and sequelæ.*—Out of the 89 non-fatal cases the following complications and sequelæ were recorded; malarial fever, twice; catarrhal otitis media, once; phlebitis of the internal saphenous, once; bronchial spirochetosis, twice; multiple neuritis of the lower extremities, once; post-typhoid psychosis, twice; cardiac and nervous irritability, once; intestinal hæmorrhage, five times.

Among the fatal cases, Group I. it will be recalled there were 3 cases of perforation and one of hæmorrhage.

#### TYPHOID FEVER AMONG FILIPINOS.

We have performed laboratory tests on 105 Filipinos suspected of having typhoid fever and obtained positive serum reactions in sixty. *Bacillus typhosus* was recovered from the stools of three of these and from the blood of two. Twenty-one of the positive results were obtained from the San Fernando epidemic, and no case histories are available. From the remainder of the 60 we received clinical records for 26 patients of whom 1 died with perforation, 1 ran an entirely atypical course, 12

apparently were received in the last week of a classical typhoid attack while the remaining 12 passed through a period of continued fever ranging from ten to thirty-nine days in length and averaging 29.6.

These last 12 cases, which on clinical grounds alone appeared to be typhoid, are included in our Group IV. considered above, but will be briefly touched on at this point in order to determine if the disease in natives differs from that seen in the white man. All but two of these natives ran a febrile course of over 19 days. The onset was gradual in all instances. Chills were noted for two patients. The temperature chart showed a well defined fastigium in seven cases and the fever ranged at the height of the disease between  $40^{\circ}$  and  $41.1^{\circ}\text{C}$ . Nose bleed occurred in three, rose spots in two, marked abdominal pain in four and tympanites in 7. Diarrhœa was noted in 4, constipation in 5 and there was no record as to bowel movements in 3. As complications, hæmorrhage occurred in two cases, post-typhoid psychosis in one and bronchial spirochetosis in two

From a study of these cases it can be said that they did not differ from typical typhoid fever of moderate and severe type as seen among white men in the United States or in the Philippines.

The atypical cases which constituted so large a proportion of the Filipino admissions in the Camp Gregg epidemic and occasionally elsewhere are of special interest because of their probable rôle in spreading and keeping up infection. We have not had enough of them under observation to make any analysis of their symptomatology profitable. Rogers found such types in 17.8 per cent of his patients in India, this percentage being much lower than was seen in our series. How commonly these atypical cases occur in the general native population is one of the unsolved problems of tropical medicine.

*Summing up the clinical aspects, we found that more than one-third of the admissions were atypical and that the well marked cases of typhoid in the Philippines, whether the patients were white or native, differed in no essential respect from the same disease as seen in the United States and Europe.* The experience corresponds in general with the findings of Rogers in India. The atypical cases were about equally common in the two races.

#### RELATION OF BACILLUS TYPHOSUS TO THE SO-CALLED UNDETERMINED FEVERS.

It seems to us that the most important point brought out by the clinical study of the cases is the frequency of occurrence in the Philippines of the short irregular and atypical forms of typhoid fever. Groups II. and III. constituted 38.7 per cent of the entire 157 cases of typhoid infection. These two classes of mild infections formed 45.6 per cent of the total admissions at Ludlow Barracks and 69.2 per cent of the admissions among the Scouts at Camp Gregg. Without laboratory examinations or the presence of a wide-spread epidemic, such as prevailed at Ludlow Barracks, few, if any, of these mild enteric fevers would have

received a correct diagnosis. This clinical type of infection with *Bacillus typhosus* may account for a considerable part of the so-called undetermined fevers met with in the Tropics, the prevalence of which in our army is shown in Tables III and IV. The sanitary importance of detecting such atypical typhoid cases is obvious.

Throughout our analysis we have been on the look-out for cases corresponding with the description of Brill's disease but have seen none suggesting that condition or the recently described Manchurian typhoid.<sup>(24)</sup>

#### DIAGNOSIS, PROGNOSIS, AND TREATMENT.

In the well-marked cases of typhoid in the Philippines the diagnosis can be made by the usual symptoms and physical signs recognized in temperate climates. In the large group of short atypical fevers diagnosis is impossible without resort to laboratory procedures. The prognosis with favorable facilities for treatment is good, the mortality for the last few years, as shown above, being about 7 per cent and no higher than was seen in the United States. The study of our series suggested nothing new in the direction of treatment. Hydrotheraphy was almost universally practiced and drugs were rarely used and only to relieve definite symptoms. The diet in general was liquid and consisted largely of tinned milk.

#### PART IV. A STUDY OF RECENT TYPHOID EPIDEMICS IN THE PHILIPPINES.

Many epidemics of typhoid fever have been recorded among troops in the Philippines before this Board began the study of the subject. The outbreaks chronicled below are ones in the investigation of which the Board took a share. The epidemic at San Fernando is of special interest in view of its occurrence in the native population of a town where there was no contact with an American garrison, the adjacent military post of Camp Wallace being occupied by native Scouts.

##### SAN FERNANDO (UNION) EPIDEMIC.

In July 1910 we learned that an epidemic fever was prevailing in San Fernando and a member of the Board (Captain Bloombergh) was sent to investigate. San Fernando has a population of 16,000 and is located on the coast about 240 kilometers north of Manila. The municipal records show that cholera visited the town in 1908 and is credited with 170 deaths. There are also recorded 34 deaths from intermittent fever, 26 from dysentery and diarrhœa and 9 from meningitis for the same year. In 1909 there are recorded 45 deaths from dysentery and diarrhœa, 12 from intermittent fever and one from meningitis. It is easy to see how typhoid may have been masked by these diagnoses during 1908 and 1909.

Statistics as to the amount of illness prevailing in 1910 were difficult to obtain. A native doctor said there were many cases and a mortality of 50 per cent. An intelligent priest reported much sickness but few deaths. An American teacher stated that out of an average enrollment of 392 children there have been 28 cases of fever with 1 death.

We obtained blood specimens from 25 persons who admitted having had the fever during the preceding 3 months. Two of these were evidently dysentery, and from the remaining 23 we obtained positive Widal reactions in 20. In addition one of the 18 specimens also agglutinated *Bacillus paratyphosus* "B" while all gave negative reactions with *Bacillus paratyphosus* "A". Thirteen other natives who furnished no history of fever gave negative serum reactions with typhoid and paratyphoid bacilli.

Cultures were made from the stools of 4 of the school children ill with a febrile disease, and *Bacillus typhosus* was isolated from two. One of these two patients gave a positive Widal reaction and from the other no blood was obtained.

The sister of this last case had died with a disease of similar clinical nature. In one house visited there had been originally 11 occupants of whom two, both children, had recently died with fever. Eight others were sick at the same time, the mother alone escaping. Of the 8 who had been ill 5 gave positive Widal reactions. These two instances show how the disease may have spread by contact but it must not be forgotten that in San Fernando, as in other Filipino towns, there is excellent opportunity for the spread of the disease by any or all of the recognized methods of infection.

Blood smears from 42 natives, including all of the cases recorded above as giving positive typhoid findings, were examined for latent malaria and no organisms were discovered.

#### FORT MILLS (CORREGIDOR) EPIDEMIC.

Three cases occurred on this island in December, 1910 and January, 1911. The first case was the wife of a white civilian employee. The next two cases were white soldiers. Two other soldiers suffering from continued fever also gave positive Widal reactions combined with negative cultural results from blood and stools. As these two men had received antityphoid vaccination, it is uncertain what the cause of their fever may have been. Several other soldiers with fever gave negative Widal reactions. A fourth case of undoubted typhoid in a native woman occurred in May, 1911.

The source of the infection in the above instances remains undetermined. The sanitary conditions on Corregidor were not favorable at that time because of the crowding and the great amount of construction going on. There was a large American garrison, a smaller force of Filipino troops and several thousand Bilibid convicts and native laborers engaged in work on the island. In addition many of the laborers had their families living in a village on Corregidor. The water supply was unsatisfactory in quantity and quality and the disposal of excreta was for the most part by dry earth closets or even more primitive methods.

#### CUARTEL DE ESPAÑA (MANILA) EPIDEMIC.

Nine cases occurred in company "M" of the 26th Infantry, all being taken sick within one week. No cases occurred in any of the 7 other companies at the post. The sanitary conditions were very good at this station and were the same for all the companies. The cook for company "M" had a short fever and gave a positive Widal reaction. It was learned that two years before in the United States he had had a fever of a month's duration followed by a relapse also lasting one month. It was thought that he might be a carrier and responsible for the outbreak in his company. However, efforts to demonstrate the bacilli in his stools and urine were unsuccessful. The men attacked were not closely associated with each other in barracks so it seems probable that contact infection was not a factor in this epidemic.

LUDLOW BARRACKS (PARANG) EPIDEMIC.

During the years 1909 and 1910 a very extensive epidemic occurred at this post, there having been 80<sup>a</sup> admissions to hospital in a period of six months beginning October 1, 1909. The official population of the post for the period averaged about 850 persons. Two cases diagnosed as typhoid occurred earlier in the year, July and August, but whether these had any bearing on the subsequent epidemic can not be determined. The admissions by months, including civilians, are as follows:

TABLE XVII.—Admissions for typhoid fever at Ludlow Barracks, Mindanao.

	1909					1910					Total.
	July.	August.	October.	November.	December.	January.	February.	March.	April.	May.	
Admissions:											
Number -----	1	1	47	3	4	3	12	*11	0	0	<sup>b</sup> 82
Per 1,000 -----			52.69	3.45	5.51	3.58	12.15	*12.64			
Mean strength of command.			892	868	726	837	988	870			

<sup>a</sup> See footnote 3.

<sup>b</sup> These figures are based on an examination of the post records and the actual clinical histories. They differ from the figures in the office of the chief surgeon, Philippines Division, which showed 4 less cases for October, 1 less for December, 2 less for January, and 2 less for March. The differences are due to certain civilians not being included in the official records.

At this point it may be of interest to note that the records of the post show that there was a small epidemic of enteric fever at Parang in 1902, the admissions having been as follows:

June, 1; August, 1; October, 4; November, 6; December, 1.

At the time of the occurrence of the 1909-1910 epidemic the sanitary conditions at the station, except for the water supply, were good. The post of Ludlow Barracks is located on an elevated, easily drained site, the grounds were well policed and the barracks and quarters were of modern construction. Excellent water closet and bath fixtures had been installed shortly before the outbreak, the outfall being in the ocean about 600 meters from the post. Flies were not common, this being the rule in the Philippines.

At the time of the occurrence of the October cases the garrison had been stationed at Ludlow Barracks for a period greater than the longest recognized incubation period for typhoid fever, even granting that the early cases had been sick a couple of weeks before the disease was discovered.

Distilled water was supplied for drinking, cooking, cleansing of the teeth, and for dish washing and its use enjoined by orders. There was no reason to think

<sup>c</sup> The Twenty-third Infantry, which formed the garrison at Ludlow Barracks during this epidemic, embarked March 20, 1910, on transport *en route* to San Francisco *via* Manila. At Manila ten suspects were transferred to the Division Hospital. Of these 4 proved to be suffering from typhoid. These should be included in the Parang epidemic, bringing the total number of cases up to 80 in six months. These 4 developing on the transport have been included in the 11 admissions for March in Table XVII.

this water was contaminated. For flushing of closets and for bathing the supply was obtained from the Nitwan river, a rapid mountain stream draining a country inhabited by Moros and but little known. The water was piped about the post and in the adjacent town of Parang which is largely frequented by the soldiers. That this water at times was used for drinking, dish washing, and cleansing of the teeth can not be gainsaid.(4)

The Nitwan river is undoubtedly extensively contaminated with fecal matter. (7) It is a custom of the Moros to defecate in running water. That typhoid fever is by no means infrequent among the natives in Mindanao seems certain from the opinions referred to near the beginning of this report and from our own work. The Nitwan water was examined at the times of the two visits made to the post by members of the Board. No typhoid bacilli were isolated from it but its bacterial count was very high and it was extensively infected with the colon bacillus. (5) (6) Examination of the dock water (piped from a spring-fed stream) and of the Alphonso XIII spring, which supplied the swimming pool, showed high bacterial counts and the presence of a few colon bacilli.

The town of Parang is a small village immediately adjacent to the post and depending for its support entirely upon the American garrison. A series of serum reactions with *Bacillus typhosus* made by this Board during the epidemic on 84 of the inhabitants of Parang gave the following results:

TABLE XVIII.—Widal tests on the inhabitants of Parang, Mindanao.

Race.	Number exam- ined.	Positive reaction.	Negative reaction.	Sick at time of test.
Chinese .....	8	1	7	0
Japanese .....	10	6	4	4
Moros .....	12	1	11	0
Hindoos .....	1	0	1	0
Filipinos .....	53	5	48	1
Total .....	84	13	71	5

The five reported sick were all suffering from a disease clinically typhoid while two others who gave positive reactions had slight fever but no other symptoms. One of the latter was Japanese and the other a Filipino. A number of these sick persons were Japanese and Filipina prostitutes and their houses were still open to soldiers while the inmates were ill and not in any way isolated.(7) The opportunities to contract infections are obvious.

Major Page, who was Surgeon at Ludlow Barracks during October, November, and December, in a report dated December 22, 1909, expressed the opinion that the epidemic was water-borne, the source of infection being the Nitwan River. He considered that the peculiar grouping of the cases in certain barracks was due to the Nitwan water supply having been first installed in those barracks, shortly before the outbreak. The evidence as to the coincidence of the dates of installing the pipes and the development of the cases in October seemed to us rather conflicting. During the later period of the epidemic, after Major Page's departure, the same peculiar grouping of cases was evident although at that time the water was installed for all the barracks.

The disease continued to occur after Major Page left Ludlow Barracks, flared up in March and April and then disappeared entirely following the departure of the 23d Infantry and a very complete and thorough disinfection of the

barracks before the new garrison entered them. This was carried out under the supervision of Major Clayton who believed the epidemic was spread by contact and not by water.

This Board made two investigations of the epidemic, one in the fall of 1909 and the other in the spring of 1910.<sup>(5)(6)</sup> From all the evidence at hand several months after the disease had entirely disappeared we concluded:

(1) That the Nitwan river was badly contaminated with human excrement and that very probably some of the cases originated from drinking this impure water at a time when it contained *Bacillus typhosus*. There was no positive evidence to show how the first cases originated.

(2) That the spread of the epidemic was due mainly to contact infection, including in this the probability of cooks or attendants infecting food while handling it in the kitchens and dining rooms. We based this opinion mainly on the following facts: (a) The vast majority of the cases for the whole period of six months were peculiarly grouped in certain barracks, one group of adjacent organizations having few or no cases while another group of contiguous buildings had many cases. (b) The cases in Parang, where unboiled Nitwan water was probably in very general use for drinking, were all among individuals coming in close personal contact with the troops. (c) No cases occurred among the officers and non-commissioned officers living in separate quarters. (d) Typhoid disappeared from among the troops at Ludlow Barracks following a change in the garrison and rigid disinfection of the buildings. The period of freedom has now been over a year.<sup>4</sup> (e) There was complete failure to suppress the epidemic by means of stringent measures based on the water borne theory.

The dates of admission of the cases to hospital largely supports the contact theory, but too much reliance should not be placed on this point since the clinical records indicate that many men had been sick between one and two weeks before going on sick report.

Efforts were made to locate typhoid bacillus carriers but without success.

A more extended discussion of some features of this epidemic can be found in the references (4), (5), (6), and (7). A "spot map" of the post and the dates of admission are on file in the offices of the Surgeon General of the Army and the chief surgeon, Philippines Division under the heading shown in reference.(6) The clinical aspects of the Parang epidemic are of considerable interest as possibly showing a rather unusually large percentage of extremely mild cases. The diagnosis in all cases was made as a result of a positive Widal reaction (1 to 50 in one hour), nearly all of these serum tests having been performed by members of the Board. None of the patients considered had ever received anti-typhoid vaccination. In several instances the blood, stool or urine cultures were positive for *Bacillus typhosus*. On many soldiers suffering from slight indispositions the Widal reaction was tried with negative results.

Including the July case and the 4 cases detected after the 23d Infantry left Parang we have clinical records of 81 patients in whom there was a positive Widal reaction. Of these three died, a mortality of 3.7 per cent. One showed at autopsy "congestion and slight ulceration" of Peyer's patches. He apparently died of overwhelming toxæmia about the 17th day of the disease. The second patient died of toxæmia on the 22d day and at autopsy showed the characteristic intestinal lesions of typhoid. The *Bacillus typhosus* was isolated from the

<sup>4</sup>Eight months after the epidemic ceased one case of typhoid was admitted to the hospital. The patient was a native. Three months later an American civilian was admitted with typhoid fever and two months after this another native, the latter coming from a neighboring *barrio*.

heart blood. The third case died of general peritonitis following perforation of the ileum. Autopsy showed enlarged and ulcerated Peyer's patches.

Forty-one cases, constituting 50.6 per cent of the whole, show on the chart a continued fever ranging from sixteen to forty days and averaging 26.4 days. The temperature charts of 33 were classed as typical of typhoid, showing a well marked fastigium which averaged 38°.8 C. in three cases 39°.4 C. in seventeen, 40° C. in twelve, and 40°.5 C. in one.

Diarrhoea was noted in 11, constipation in 21 and regularity of the bowels in 9. Rose spots were recorded in 7 cases and dicrotic pulse in 6. Complications occurred in the shape of multiple peripheral neuritis in one and post-typhoid psychosis, requiring transfer to the United States, in another.

In this group of 41, *Bacillus typhosus* was recovered from the blood of two, the stools of two and the urine of one.

The records of 27 of the cases (constituting 33.3 per cent of the whole) showed temperature curves which resembled the last week or ten days of a typical typhoid chart. In one of these 27 cases *Bacillus typhosus* was isolated from the stool, in another from the urine. It is believed that these patients had been suffering from a mild attack of typhoid fever for periods ranging from five to fifteen days before admission to hospital.

A third group consisting of 10 cases (12.3 per cent of the whole) presented trivial rises of temperature lasting for a few days and bearing no resemblance to the classical typhoid fever chart. All showed clear-cut serum reactions and from the stools of 3 the *Bacillus typhosus* was recovered. There is no reasonable doubt that all were suffering from extremely mild and atypical typhoid fever, or else were just at the end of an attack which had never caused them to be excused from duty. Their actual appearance on sick report was not due to their own volition but was the result of the general taking of temperatures and admission to hospital of all who showed any degree of fever.

Of the 81 cases considered above 3 were natives and the remainder Americans. The total number considered (81) does not include the 5 cases in the adjacent town of Parang and referred to in Table XIX.

Taken as a whole, the epidemic was characterized by constipation; absence of haemorrhage, very slow pulse, rarely over 100 and often normal, by a large ratio of very mild or ambulatory cases, and by a low mortality, 3.7 per cent. An analysis of the October epidemic was made by Lieutenant Charles T. Dulin and of the whole period of the epidemic by Lieutenant Clarence E. Fronk.

#### CAMP ELDRIDGE (LOS BAÑOS) EPIDEMIC.

Eleven cases of typhoid fever occurred at this post during July and August, 1909, the garrison consisting of 4 companies of the 7th Infantry. The cases were quite evenly distributed. One patient was a commissioned officer and of the 10 enlisted patients 4 came from "C" company, 3 from "A" company, 2 from "B" company and 1 from "D" company.

The post of Los Baños is situated on an elevated, well-drained site. The earth closet system was in use at the time of the epidemic. The water for drinking purposes was boiled. That for bathing is derived from a stream, the intake being a considerable distance up on Mount Makiling. The possibility of its having been infected can not be excluded. An effort made at this laboratory to find carriers among the company cooks or elsewhere in the command was unsuccessful. The garrison left Fort Wayne, near Detroit, (where typhoid is said to have been common) on April 30, 1909, and arrived at Camp Eldridge on June 6, 1909. The first case of typhoid fever entered hospital July 3, 1909. A study of his chart and of the charts of the next two cases, admitted July 9 and



10 respectively, would indicate that the patients came into the hospital in the first few days of their typhoid course. It appears, therefore, that the infection of these first cases was gained after the troops arrived at Camp Eldridge. As far as could be learned, there was no typhoid fever in the adjacent town of Los Baños except for the case of a soldier who while on furlough had been living at the hotels in Los Baños and developed typhoid there. He subsequently died of the disease in the Division Hospital.(8) The ice and bottled waters produced by a commercial company in Los Baños fell under suspicion, since they were in use among the soldiers. Samples of the bottled products examined by the Bureau of Health in Manila were negative for the bacillus of Eberth.

It was found impossible to locate the origin of the epidemic. Its manner of spread was not definitely determined but was very probably due to flies which were numerous at that time and may have carried the organism from the dry earth closets infected by the first case.

Of the 11 cases reported as typhoid 10 presented temperature charts with febrile periods ranging from twelve to forty-one days and averaging 23.1 days. All but one of these showed a well-marked fastigium. From the blood of 4 the *Bacillus typhosus* was isolated, four others gave positive Widal reactions and in the two remaining cases no Widal reaction was performed but the diagnosis was clear on clinical grounds.

The eleventh case diagnosed as typhoid is of a doubtful nature. The temperature curve is not characteristic and one Widal reaction and one blood culture, both done on the 11th day, were negative.

A large number of mild cases of fever occurring in the command at the time were negative for Widal reaction and blood culture at the Laboratory of the Board for the Study of Tropical Diseases. As dengue was epidemic in the post at the same time as the typhoid outbreak, the number of cases requiring laboratory observations was considerable.

The progress of the disease in this epidemic was characterized by lassitude, headache, constipation, rose spots, enlarged spleen and dicrotic pulse. The charts indicate that constipation existed in 7 patients, regularity in 1, and abnormal frequency of bowel movement in two. Abdominal pain was marked in one case, delirium in another and intestinal hæmorrhage in two. There were no deaths.

#### CAMP GREGG (BAYAMBANG) EPIDEMIC.

Fifteen cases of typhoid are recorded among the Philippine (native) Scouts at this post between November 26, 1909, and April 5, 1910. Thirteen of these gave positive Widal reactions at the laboratory of the Board. As the other two had an irregular fever and as Widal and stool cultures were negative, we have excluded them from consideration.

This epidemic is of much interest because the entire command at this post is native with the exception of the commissioned officers and a half dozen non-commissioned staff officers.

The post is built on a slight elevation, located in a broad, poorly drained plain. The region is very malarious. The barracks are in rather poor condition. Fæces are disposed of by the dry earth closet system. Flies are not common. Drinking water is distilled. Water for bathing is piped over the post and drawn from the Agno River, a muddy and badly contaminated stream. There is no doubt that the Scouts frequently drink this water in the post and in the town of Bayambang, which adjoins the post. Lieutenant Huber in his report of the epidemic expresses the opinion that typhoid is constantly present in Bayambang and states that he has seen several cases in the families of Scouts living in the town.

The clinical histories of these cases are very meager, but the charts show some points of interest. Two of the cases are classed as typical typhoid, the febrile course being at least twenty days in one and nineteen in the other. There was a well-marked fastigium. One case had a relapse of twelve days' duration and the other a post-typhoid psychosis. Two others might have been diagnosed clinically as very mild typhoid, the febrile period after entry to hospital being between ten and twelve days and the temperature curve not typical. The nine remaining cases showed fever for a week or ten days and may well have been either entirely atypical or the last portion of a typical typhoid chart.

The stools during convalescence were negative in these thirteen cases and cultures from small quantities of blood taken from several in the earlier part of the disease were negative. The specific diagnosis of typhoid rests solely on positive agglutination reactions with *Bacillus typhosus*. We might question the certainty of this method of diagnosis in the atypical cases were it not for the following points: (a) Two of the cases gave first a negative reaction followed a few days later by a positive one. (b) Many Scouts at the post during the same period who were suffering from mild fevers reacted negatively. (c) We have done Widal's on several hundred healthy natives and only rarely have obtained a positive reaction.

The writer as representative of the Board at the present time, wishes to acknowledge his obligations to the many medical officers at the Division Hospital and throughout the Philippine Islands who have furnished the materials for the laboratory studies and the clinical records for the analysis, and also to the former members of the Board who did a large part of the laboratory examinations on which this report is based.

#### PART V. CONCLUSIONS.

1. Typhoid is a widely scattered and common disease in the Philippines; its incidence in Manila is above the average rate for the United States and is exceeded by only a few of the worst American cities; the average admission rate among American soldiers in the Philippines exceeds that for the troops serving in the United States; medical officers from many regions report its frequent occurrence among the Filipinos.

2. The statistics from the Filipino (native) Scouts show a much lower typhoid rate than for white troops, possibly due to failure to diagnose the atypical cases.

3. Widal reactions performed on the blood of 591 healthy Filipinos suggest a comparatively recent attack of typhoid in about 6 per cent of adults, but do not indicate that the disease is prevalent in childhood.

4. Many epidemics have occurred among soldiers in the Philippines and three outbreaks among natives have been studied. Epidemics of great severity among the Filipinos are either rare or unnoticed.

5. The occurrence of the disease in the Philippine Islands is quite evenly distributed throughout the year. The incidence is least in the second quarters.

6. The appearance of the Widal reaction in typhoid fever in the Philippines is not as a rule delayed.

7. Paratyphoid organisms are occasionally isolated in the Philippines.
8. The leucocyte count in typhoid remains normal for whites and is slightly increased for natives. The differential count is normal for both races.
9. The mortality for white troops in the Philippine Islands during the last five years has been no higher than at home. It appears somewhat higher for Filipinos but this may be due to failure to diagnose all the mild cases.
10. More than a third of the cases of enteric fever, whether among Americans or Filipinos, are entirely atypical and can not be diagnosed without laboratory methods.
11. Over one-half of the cases occurring in the Philippine Islands can be diagnosed clinically and differ in no essential particular from typhoid fever as seen at home. This is true for both American and Filipino cases.
12. Much work still needs to be done among the natives to estimate the actual amount of mild and atypical typhoid which is occurring and to determine why extensive and destructive epidemics are not more often seen.

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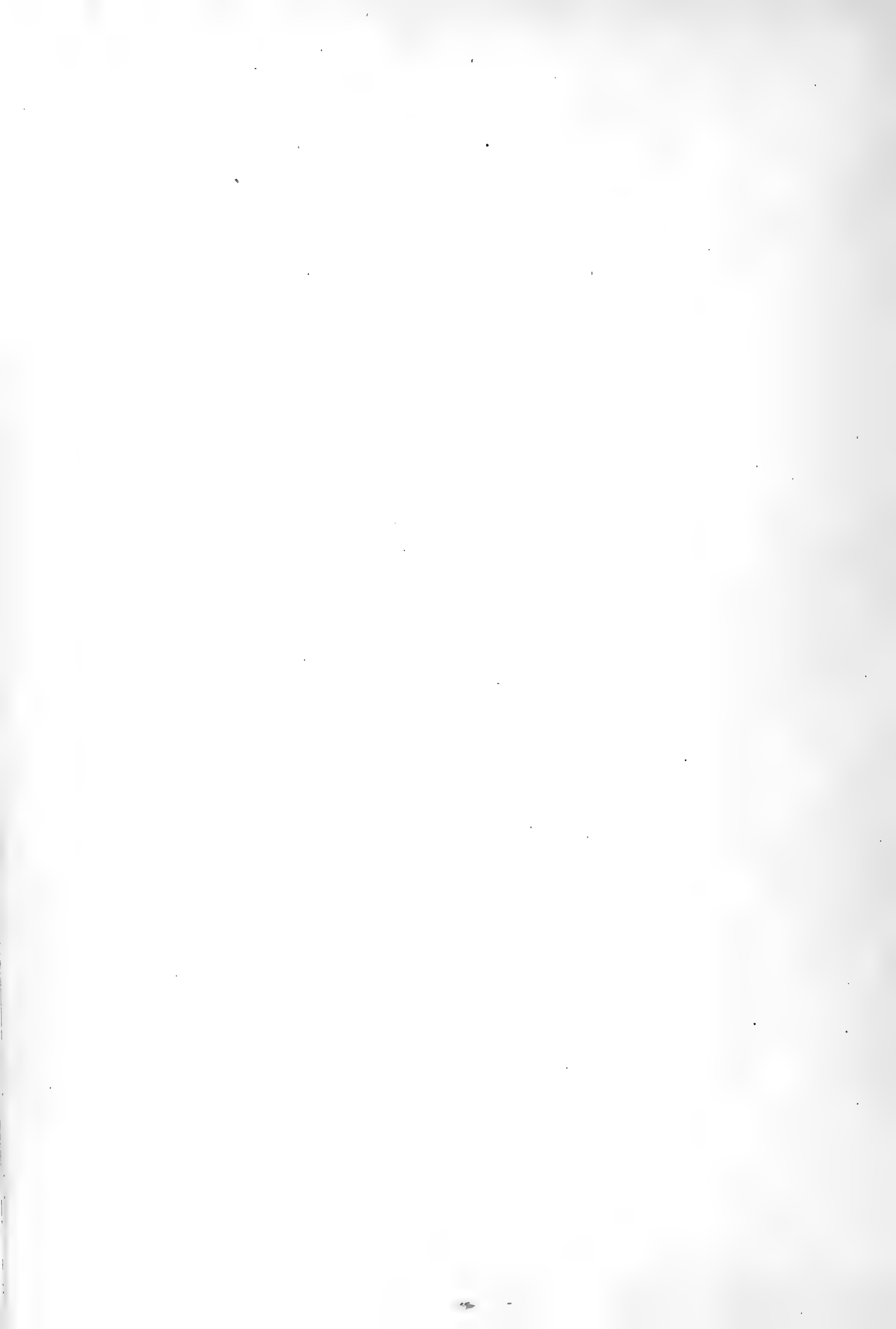
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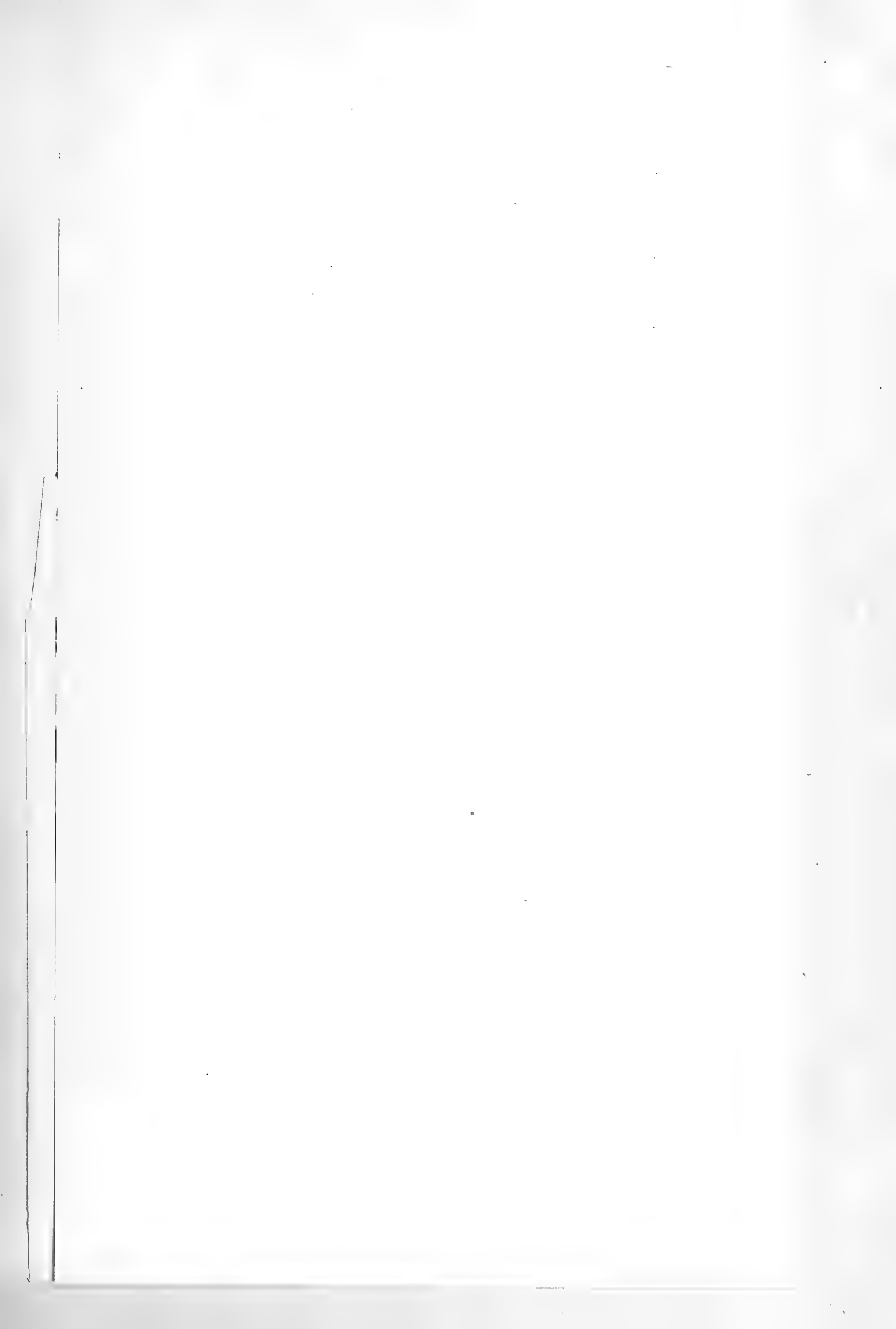
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## ILLUSTRATION.

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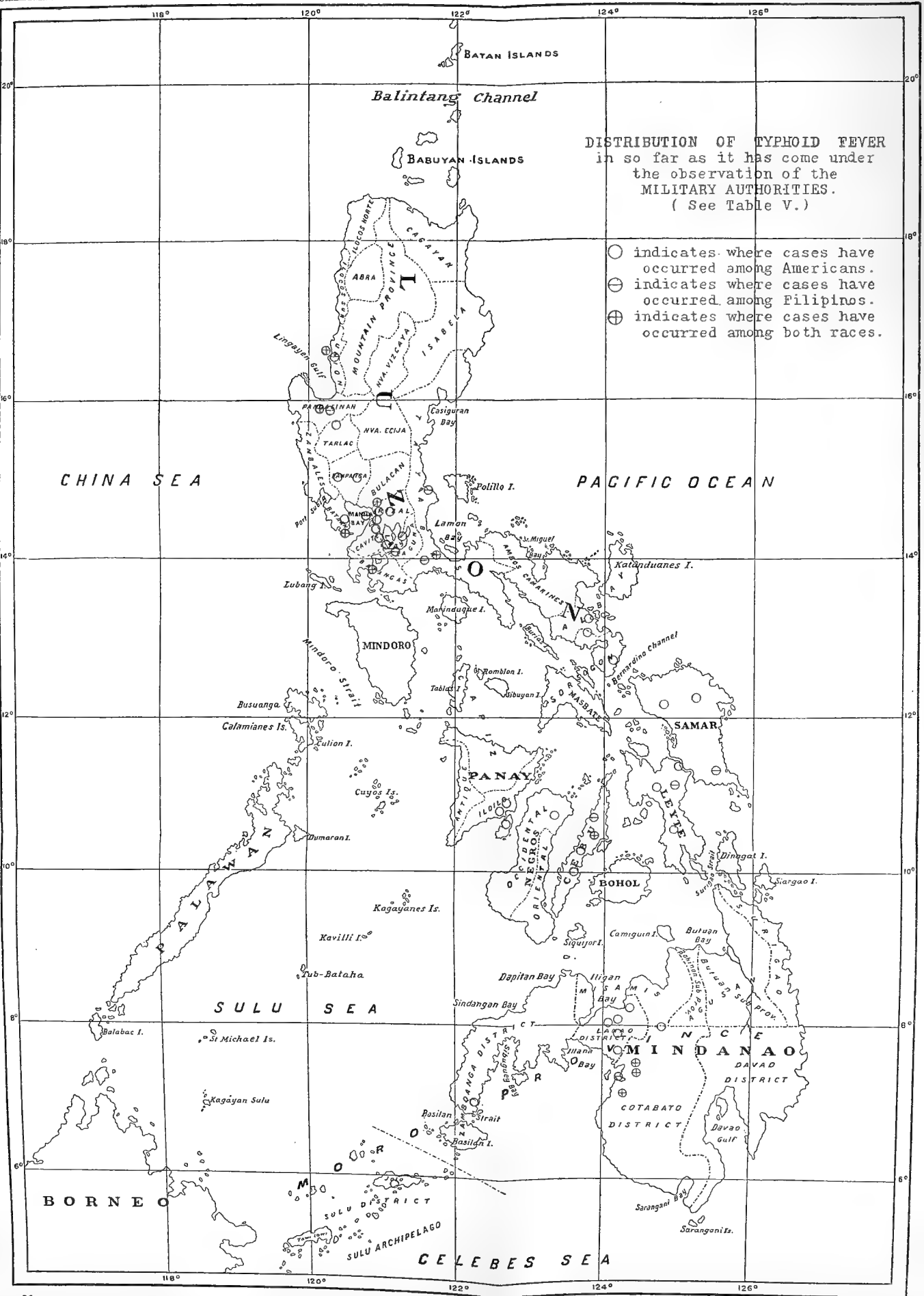
Map showing the distribution of typhoid fever in the Philippine Islands in so far as it has come under the observation of the military authorities.











MAP SHOWING THE DISTRIBUTION OF TYPHOID FEVER IN THE PHILIPPINE ISLANDS IN SO FAR AS IT HAS COME UNDER THE OBSERVATION OF THE MILITARY AUTHORITIES.



## THE WASSERMAN REACTION IN SYPHILIS, LEPROSY, AND YAWS.<sup>1</sup>

By HORACE D. BLOOMBERGH.<sup>2</sup>

*(From the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.)*

These observations were undertaken with a view of determining if the Wasserman reaction could be obtained in certain tropical diseases in which it has been reported by some authors to be positive. Owing to a scarcity of material at the time the work was being done we were able to examine only two cases of yaws. The methods we employed for making the tests followed in general the original procedure of Wasserman except as regards the antigen, which was prepared from normal guinea-pig heart.

Sheep are not slaughtered in Manila and fresh sheep's blood from different animals can not therefore be obtained. The cells used in all our tests were obtained at different times as needed from the blood of the same sheep. Only during the last series of tests did the suspicion arise that the sheep had been bled too frequently, and therefore the cells were fragile and less resistant than usual to the combined influence of amboceptor and complement. The cells were thoroughly washed and used on the same day as prepared. The dose was 1 cubic centimeter of a 5 per cent suspension in 0.85 per cent salt solution.

The complement was the serum of a guinea pig killed on the day of the test. In this factor we found great variation in concentration. At times the serum was found to be almost devoid of complement. On several occasions we attempted to preserve the complement by the addition of sodium chloride according to the method of Hecht<sup>(1)</sup> but without good results. The dose of the complement was 0.1 cubic centimeter, or, as employed in actual practice, 1 cubic centimeter of a 1:9 dilution, in salt solution.

The hæmolytic amboceptor was the inactivated serum of a rabbit which had been immunized by successive doses of well-washed sheep cells. As a rule, we have used the amboceptor in the dilution of 1:600. Our practice has been to take at least twice the amount which, with 0.1 cubic centimeter of complement, completely hæmolyzed 1 cubic centimeter of a 5 per cent suspension of blood cells in one hour, requiring, however, complete hæmolysis with the quantity used in

<sup>1</sup> Read, by permission of the Chief Surgeon, Philippines Division, before the Eighth Annual Meeting of the Philippine Islands Medical Association at Manila, P. I., February 22 to 24, 1911.

<sup>2</sup> Major, Medical Corps, United States Army.

one-half hour. The invariable dose was one cubic centimeter of the diluted serum. The amboceptor has remained stable for over four months, preserved after inactivation in sealed ampoules.

The blood serum of the patients as a rule was removed from the veins at the bend of the elbow on the day preceding the test and the serum from the clot was inactivated on the same or following day. It was found later that 0.6 or 0.8 cubic centimeter of serum could be obtained from the blood removed by deep puncture from the finger and collected in small tubes. The serum resulting from the clot was centrifugalized and later placed in similar small tubes, floated on corks in water and inactivated. All inactivation was done at 55° to 56° C. for one-half hour. The serum at first was tried in the two doses of 0.1 and 0.2 cubic centimeter diluted with the necessary quantity of salt solution. Later the dose of 0.2 cubic centimeter was used exclusively.

The antigen was made by grinding guinea-pig heart together with sand in a mortar and adding to this 50 cubic centimeters of 95 per cent alcohol. This was heated to 60° C. for two hours, shaken from time to time, and then filtered. The dose was found to be 0.1 cubic centimeter, twice this amount inhibiting hæmolysis. The antigen has apparently remained a constant factor.

The actual technique of the reaction as carried out by us does not differ from that usually employed. On all occasions on which the reaction was made, a positive syphilitic and a normal serum were used as the main controls of the effective specific action of our reagents. The sera were likewise tested to determine whether they, independently of the antigen, bound the complement or whether they were actively hæmolytic with cells alone, or in the presence of complement. While it was found in actual practice that one hour was a sufficient length of time for the reaction, the final reading was always made at the end of two hours after the addition of the hæmolytic amboceptor and red blood cells.

At the time of our preliminary titration to establish the strength of our amboceptor, we made controls of cells plus complement, amboceptor and antigen, to show that the antigen did not inhibit hæmolysis; and of cells plus complement and of cells plus amboceptor to show that hæmolysis did not occur under these conditions.

It is to be noted first of all that the results reached by us depend on the action of an antigen derived from normal heart and the question of the specificity of action of our antigen comes immediately into question. For our tests we have been unable to obtain syphilitic foetal organs in the city of Manila, and we may add that the work of others being conducted along lines similar to our work at the present time in Manila, is likewise undertaken with a similar antigen from normal organs. In July, 1910, Wasserman<sup>(2)</sup> still advocated the use of syphilitic organs in the preparation of the antigen and the good results reached by Dean<sup>(3)</sup> on the reaction in idiots, referred to by Wasserman in his address, might indicate that in certain lines of research such an antigen is still a necessity. Bayly<sup>(4)</sup> used an alcoholic extract of rabbit's heart and obtained as good results as with an alcoholic extract

of foetal syphilitic liver. The question is far from being decided but the weight of evidence would seem to indicate that extracts of syphilitic organs are not superior as specific antigens to the extracts of normal organs.

In all, 95 cases have been examined by us. Of these the following 76 gave negative results:

*Seventy-six cases showing negative Wasserman reactions.*

Num- ber of cases.	Clinical condition.	Num- ber of cases.	Clinical condition.
18	Leprosy.	1	Exophthalmic goitre.
17	Syphilis or suspected syphilis.	1	Otitis media chronio.
9	Syphilophobia.	1	Pemphigus.
5	Dysentery, amœbic, chronic.	1	Rheumatism, muscular.
2	Dysentery, amœbic, acute.	1	Gastritis, alcoholic.
1	Dysentery, bacillary, acute.	1	Neurasthenia and syphilopho- bia.
2	Rheumatism, articular chronic.	2	Dengue.
1	Iritis.	1	Ulcer of the leg.
1	Malaria, tertian, acute.	1	Fever, type undetermined.
1	Rodent ulcer.	1	Osteoma of the tibia.
1	Liver abscess.	6	Healthy Filipinos.
1	Suspected leper.		

It will be observed that in the above list a certain number of cases are tropical diseases of a protozoal or presumably protozoal nature. It was our desire to work particularly on the reaction as applied to tropical diseases, but we have failed to obtain the material which we most desired.

Apart from the syphilitics enumerated in the table our negative results have not been disappointing, and are entirely in agreement with our ideas of the results of Wasserman reactions properly carried out. Many of the cases were taken from the ward for normal controls, but on account of the habits in general of many of our patients, we habitually used several normal controls at each examination.

Certain cases were examined for purposes of diagnosis, notably the two following:

A case of ulcer which gave a history of a sore of eighteen months' duration on the dorsum of the nose. The first examination made of this patient's serum showed a slight inhibition of hemolysis; subsequent examinations proved that the case was negative. Long continued mercurial treatment had no effect on the condition, and the case was considered to be one of rodent ulcer.

A case of osteoma of the right leg, which gave a history of a chancreoid or soft sore on the penis in 1901 and no history of secondaries or any other symptom or sign of syphilitic infection. The man noticed a swelling of the right shin in 1905 and states that occasionally it aches but as a rule he had no trouble in any way due to its presence. The soldier is married and his wife has two healthy children. Until the Wasserman test was used it was thought the tumor was very probably a syphilitic periostitis.

The seventeen cases in which clear luetic histories were obtained, but which gave a negative Wasserman reaction were, to a certain extent, disappointing, although the results were not out of accord with the findings of some other observers, as will be shown in the discussion a little further on. The three following are of interest among the syphilitics who gave negative reactions.

One case was a patient who had severe general rupial lesions and whose serum was examined one week after the administration of Salvarsan ("606"). The case reacted negatively. However, it must be stated that the patient had been for a long time on very vigorous treatment with mercurials. He had not previously been examined with the Wasserman reaction because of our frequent negative results in cases under treatment.

Another, which had been under mercurial treatment only three or four days reacted negatively. This soldier originally had a chancre in the inner canthus of the eye in which one of the Board had demonstrated *Treponema pallidum*. The reaction was made shortly after the appearance of a rash. Whether the absence of the reaction was due to an insufficient liberation of antibodies, or to the treatment received we are of course unable to say.

A third case of more than passing interest was that of right-sided hemiplegia. This undoubtedly was a syphilitic condition occurring as it did in a young man who gave a history of a typical primary lesion, the usual secondaries, an iritis, and finally, almost two years after infection, a hemiplegia with aphasia. This patient had been thoroughly under treatment with mercurials and iodide, particularly for the month or so preceding transfer to the Division Hospital. The Wasserman reaction was negative. That the condition was really syphilitic was demonstrated to our satisfaction by the marvellous improvement which the patient showed after treatment with Salvarsan.

The remaining fourteen syphilitic cases which gave negative reactions had all been under treatment for several months.

A symposium on the theory and workings of the Wasserman reaction was held at the Seventy-eighth Annual Meeting of the British Medical Association; and on this occasion Wasserman<sup>(2)</sup> made some statements which are pertinent at this point. He said exhaustive investigations have shown that in the majority of recent cases we can cause the disappearance of the reaction through quicksilver treatment. Ehrlich's new arsenic preparation appears to cause in a higher percentage the disappearance of the reaction; whether permanently or not can not yet be decided.

Mulzer,<sup>(5)</sup> working both with the original Wasserman procedure and with a modified method, has demonstrated that during a mercurial course the serum reaction may change frequently from positive to negative and again to positive at intervals and concludes that it can not be used to determine the sufficiency of a cure, and that for diagnostic purposes it should not be utilized during or immediately after a course of mercurial treatment.

It is useless to repeat the various reports in the literature which show the poor results that are obtained in attempting to secure positive reactions with treated cases of syphilis. Harrison<sup>(6)</sup> quotes various authors who have proved that heated serum loses its deviating power to a certain extent. He found that after heating for ten minutes at 55° C. the complement for hæmolytic amboceptor was lost and that in *well-treated* latent cases a considerably higher percentage of positive results were obtained by this method than with the same serum

heated for thirty or sixty minutes respectively. If this is confirmed, an improved technique in this direction may result for the investigation of the sera of treated cases. We note in his table of results(7) the statement that of 151 cases of secondary syphilis, 136 were positive; 15 were negative, and, in a footnote, he says that 13 of these negative ones had received at least one course of inunctions or injections.

The following is a list of our twenty cases which gave a positive Wasserman reaction.

*Twenty cases showing positive Wasserman reactions.*

Num- ber of cases.	Clinical condition.	Num- ber of cases.	Clinical condition.
5	Syphilis secondary.	1	Dementia præcox.
7	Syphilis tertiary.	1	Periostitis, chronic.
3	Leprosy.	1	Rheumatism, acute articular (probably syphilitic).
2	Yaws.		

The small percentage of positive results obtained by us in cases of leprosy was referred to briefly in the last quarterly report of the Board. We stated then that 18 out of 21 cases were negative, and that of the three positive, one gave a clear history of syphilis of seven years' duration. The two remaining positive cases passed from observation and we unfortunately were unable to make inquiry from them as to the existence of syphilitic infection or infection with yaws at some previous time.

Wechselmann and Meier(8) have recorded one case of leprosy in which the reaction was positive, using extract of syphilitic liver. The case had originally been considered syphilitic, but later lepra bacilli were demonstrated in the lesions.

Eitner,(9) after having obtained a positive reaction in a case of leprosy with a watery extract of leprous tissue, later secured in a second case a positive reaction using as an antigen an alcoholic extract of normal guinea-pig heart.

Cases referred to frequently in the literature are those of Slatineanu and Danielopolu.(10), (11) Their first report referred to 26 cases of leprosy examined by means of leprous antigen and of these 20 were completely positive and 4 more were reported positive, although the complement fixation was less complete. With alcoholic extract of syphilitic liver their results were different. Of 21 cases examined, 11 were "completely positive," 5 apparently less so, and the remainder negative. At present the general tendency of workers on the Wasserman reaction is to deal with positive and negative reactions only, although occasionally the importance of partial reactions is emphasized. In this connection we might add that almost invariably our results have been distinctly positive or negative and only in rare instances has there been a partial arrest of hæmolysis in negative cases.

Baermann and Wetter,(12) working in Sumatra, found that there was about 7 per cent of manifestly syphilitic individuals present among their laborers and that about 20 per cent of apparently healthy workmen gave a positive Wasserman reaction. Their percentage of positive reactions in leprosy varied between 50 and 65 per cent, the difference depending upon the type of leprous lesions present. Syphilitic antigen was used in their tests.

From our own limited experience we consider it doubtful if a positive Wasserman reaction is to be obtained as a result of infection with the *Bacillus lepræ*. Before attributing a positive reaction in a leper to his leprosy alone it is necessary to consider the possibility not only of syphilitic taint but also of present or antecedent frambœsia. This latter is especially important when working with leprosy in those parts of the Tropics where yaws is prevalent. Recently, we have seen a Filipino leper who also showed typical lesions of yaws.

In yaws we were able to make observations on only two individuals. The serum of one case was forwarded to us by Lieutenant J. R. Barber, Medical Corps, from Corregidor Island, and came from a young Filipino adult in the active stage of the disease. The diagnosis was based on the clinical appearances and on the presence of *Treponema pertenue* in the nodules. The second serum was obtained from a ten-year-old boy who had long been a frequenter of the skin clinic at St. Paul's Hospital in Manila. Both of these sera gave the same strong inhibition of hæmolysis that we obtained from our untreated syphilitic cases. The finding confirms the results of many others who have tried the serum reaction on yaws. It will be of interest to add that seven days after treatment with "606" in the Philippines General Hospital, to which we had transferred the boy and where we obtained the blood a second time through the courtesy of Dr. Donald Gregg, the serum reaction of the second case remained positive. Evidently the time was not sufficiently long for the substances in the blood arising from the activities of the *Treponema pertenue* to disappear. Incidentally, the recovery in this case was remarkably rapid, although the boy had done very poorly on the iodide of potash treatment given him at the clinic over a period of more than a year.

Of the syphilitic cases which gave positive serum reactions few had ever been on mercurial treatment and not one had been recently treated. Four cases gave negative histories of previous syphilitic infection and in two the diagnosis could not have been made without the aid of the Wasserman reaction.

One patient had been transferred to the Division Hospital with the diagnosis of chronic periostitis, cause unknown, and had been on sick report at intervals during the preceding eight months, the total period of disability being more than three months. The diagnosis of syphilis was made by us on the strength of a positive Wasserman reaction. The condition began to improve shortly after the inauguration of mercurial treatment and the soldier was subsequently returned to duty.

A second man, "C. P.," had been transferred to the Division Hospital with the diagnosis of malarial fever after a considerable time on sick report. There were no signs or symptoms in this case other than the presence of fever, and the serum was tested in the expectation of obtaining a negative result. The



reaction was positive. The therapeutic test confirmed the diagnosis of syphilis as the febrile condition disappeared promptly on the institution of mercurial treatment.

The third case gave a history of previous syphilis. One thumb, showing rupial ulceration, had been removed on account of the resemblance of the lesion to carcinoma, and the failure of the condition to improve on mercurial treatment. This case gave a good Wasserman reaction in spite of previous treatment with mercury and after an intravenous injection of Salvarsan, the rupial condition, which was then general, disappeared promptly.

Altogether the Board has been pleased with the practical results of the Wasserman reaction and it is a matter of regret that we were unable to make a wider use of it in our study of tropical diseases because of difficulty in securing suitable material at this time.

In conclusion, acknowledgment is made to the various officers of the Division Hospital, particularly Captain Snyder and Lieutenant Shields, from whose wards the majority of our patients were secured, for kindly coöperation and many courtesies extended.

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## REVIEW.

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**Practical Bacteriology, Blood Work and Animal Parasitology including Bacteriological Keys, Zoological Tables and Explanatory Clinical Notes.** By E. R. Stitt, A. B., Ph. G., M. D., Surgeon, U. S. Navy; Graduate London School of Tropical Medicine; Associate Professor of Medical Zoölogy, Philippine Medical School. \* \* \* Second edition revised and enlarged with 91 illustrations. Cloth. Pp. 345. Price, \$1.50. Philadelphia: P. Blakiston's Son & Co., 1910.

The reviewer's prejudice against all pocket manuals is strong. As a rule they contain nothing but what may be had in the larger works, and in the attempt to abridge it becomes a task to know what to omit and what to include. As a result many important facts are omitted, others are only partially stated, if not actually given a wrong setting, and hence the student receives a wrong conception of the actual facts in the case.

While the volume under consideration is no exception to the above criticisms, still it contains some things that the student will not readily find elsewhere. It is more than a compilation of facts from larger works. The author has drawn extensively from his wide experience as a clinical laboratory worker and teacher, both in the temperature zones and in the Tropics, which gives the book a different setting from the ordinary pocket manual, and forms the real worth of the volume. The reviewer would not recommend it as a text-book, but the busy interne in the hospital and the practising physician would find it helpful and suggestive.

V. L. A.



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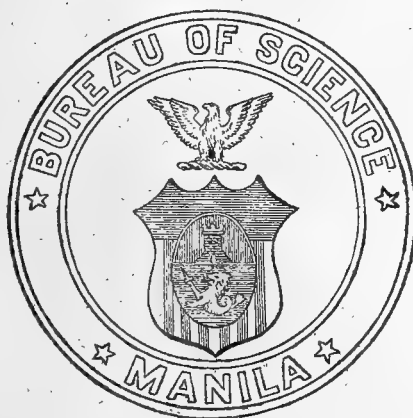
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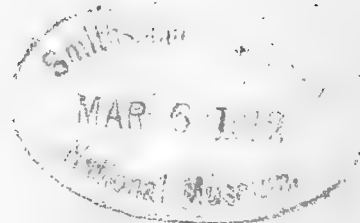
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## ADDISON'S DISEASE AND ADRENAL TUBERCULOSIS.

---

By B. C. CROWELL.

*(From the Pathological Laboratory of Bellevue Hospital, New York, and the  
Biological Laboratory, Bureau of Science, Manila, P. I.)*

---

### INTRODUCTION.

Extensive clinical, pathological, and experimental investigations into the pathogenesis of the symptom-complex described by Addison have to a large extent failed to elicit any more positive knowledge of the subject than was originally possessed by that author. Universal recognition has been accorded the establishment of the symptom-complex of asthenia, anæmia, pigmentation of cutaneous and mucous surfaces, with nervous and gastro-intestinal disturbances as a clinical entity, and its frequent association with destruction of the adrenals by tuberculosis. However, the problems of the pathological anatomy and physiology of this disease have become increasingly difficult proportionately to the number of its investigators.

That Addison's disease and tuberculosis of the adrenals are frequently associated and that there is some causal relationship between them is generally admitted; still the occurrence of apparently unequivocal cases of Addison's disease without adrenal destruction, and cases of adrenal destruction by various causes without the appropriate symptoms, has furnished many difficulties in the solution of the problem. In 370 cases

of typical Addison's disease collected by Lewin,<sup>(1)</sup> sound adrenals were found in 12 per cent and diseased ones in 88 per cent.

Typical cases of Addison's disease associated with destruction of the adrenals by causes other than tuberculosis are not infrequent. Some of these have been collected in a recent survey of the literature.

*Simple atrophy* of the adrenals has been found in Addison's disease by Goldschmidt<sup>(2)</sup> (one case), Philips<sup>(3)</sup> (one case), Karakascheff<sup>(4)</sup> (five cases), Marchand<sup>(5)</sup> (one case), Bittorf<sup>(6)</sup> (three cases), Roloff<sup>(7)</sup> (one case), and Bramwell<sup>(8)</sup> (one case).

*Complete aplasia* of the adrenals was reported in one case by Bramwell.<sup>(9)</sup> *Amyloid degeneration* has also been assigned as the cause in one case by Bittorf.<sup>(10)</sup>

*Tumors of the adrenals* in association with Addison's disease have been recorded by Bittorf<sup>(10)</sup> (two cases, hypernephroma) Marchand,<sup>(11)</sup> (one case, hypernephroma), and Fleiner<sup>(12)</sup> (one case, sarcoma).

*Thrombosis of the adrenal veins* has been described as the cause of acute Addison's disease by Simmonds<sup>(13)</sup> (one case), Straub<sup>(14)</sup> (one case), and Bittorf<sup>(10)</sup> (one case).

*Pressure on the splanchnic nerve* by an aneurism of the abdominal aorta was reported in one case by Jürgens.<sup>(15)</sup> This case is of interest as suggesting the splanchnic nerve as bearing a trophic relation to the adrenals. Dreyer,<sup>(16)</sup> Tschoboksaroff,<sup>(17)</sup> and Asher<sup>(18)</sup> have proved that the major splanchnic is the secretory nerve of the adrenals and that the vagus has no influence over the adrenal secretion.

Instances of adrenal destruction without Addison's disease are also numerous, and in many of these the adrenals are the seat of tuberculosis.

V. Kahlden<sup>(19)</sup> has recorded 6 cases of caseous adrenals without Addison's disease.

Wiesel<sup>(20)</sup> reported a case of a 16-year old girl who had no clinical symptoms of Addison's disease although extensive tuberculosis of the adrenals was present.

Goldschmidt<sup>(2)</sup> reported 2 cases of tuberculous adrenals without Addison's disease.

Lewin<sup>(1)</sup> mentioned 44 cases of destruction of the adrenals by various causes in patients showing no evidence of Addison's disease during life and dying of intercurrent affections.

Karakascheff<sup>(4)</sup> has drawn attention to cases of old hæmorrhage destroying the adrenal medulla without the production of Addison's disease and records an example of this in a child 5 months old.

Although tumors in the adrenal are occasionally associated with Addison's disease, as noted above, yet most frequently they cause no clinical manifestations suggesting it. The reason for this may possibly be due to the infrequency of destructive bilateral tumors.

These cases, which have been selected from a very abundant literature on the subject as typical of the difficulties presented, serve to show the complexity of the problem. Such cases form in part the basis for explanatory theories. However, they are insufficient without a knowledge of the findings outside of the adrenals, which, I think, can best be considered in a general discussion of the subject.

As an introduction to this, a brief sketch of the development of the adrenals is given.

The cortex of the adrenal is developed from the mesodermic epithelium which covers the mesial aspect of the forepart of the Wolffian body, in front of the germinal epithelium. Masses of sympathetic formative cells exist between this primitive adrenal and the aorta, groups of which grow into the adrenal and eventually form the cells of the medulla. These cells increase in size, their nuclei become enlarged and vesiculated, and they acquire the property of staining brown with chromium salts. However, not all of these formative cells enter the adrenal; many remain along the course of the sympathetic nerves in the abdomen and there undergo the same change into chromophil cells. These cells were termed "chromophil cells" by Stilling,<sup>(21)</sup> "chromaffin cells" by Kohn,<sup>(22)</sup> and "phäochrome cells" by Poll.<sup>(23)</sup> Granules or globules of a substance yielding this reaction have been described in the blood within the medullary sinuses and in that of the suprarenal vein. This forms strong histological evidence that the medullary cells pass a secreted substance into the blood.

#### PATHOGENESIS OF ADDISON'S DISEASE.

A year after his original communication, Addison himself found changes in the abdominal sympathetic in certain cases, and from that time until the present there has been constant discussion as to whether the lesions of the sympathetic system or adrenals are responsible for the symptoms. Experiments directed toward the production of Addison's disease by adrenal enucleation succeeded in reproducing all the clinical symptoms except pigmentation, which was not evident during the brief period that the experimental animals lived.

Neusser<sup>(24)</sup>, from a consideration of the cases previously reported and from what was then known of the physiology of the adrenals and sympathetic system, promulgated the following theory: "The suprarenal gland is a gland with an internal secretion. It possesses a double function: first, the neutralization of the toxic products of the metabolic activity of other organs; second, the synthetic production of a substance which is essential to the sympathetic system, maintaining its nutrition and a normal tone. In every case the symptoms of Addison's disease result from impairment, or eventually complete suppression, of these functions of the suprarenal capsules, brought about by disease of the capsules themselves, or of the nerve tracts controlling their functions. These nerve tracts extend from the spinal cord through the splanchnic nerve and the celiac ganglion. This impairment and eventual suppression of the function of the suprarenal capsules account for the nutritive and functional disturbance of the sympathetic system, on the one hand, and for the general autointoxication, on the other. In addition to these two principal factors, extension of the pathologic process in many cases to the abdominal sympathetic is responsible for the occurrence of some of the symptoms of Addison's disease. Pigmentation of the skin and mucous membranes is not an integral part of Addison's disease, and, though of decided diagnostic significance, is not an essential feature. It is rather an indirect than a direct suprarenal symptom, arising only through the agency of local or general disease of the sympathetic system." The antitoxic property of the adrenal cortex lacks definite proof.

Previous to this time numerous observers had reported the presence of changes in the spinal cord, spinal ganglia, and splanchnic nerves.

It has been known since the time of Henle<sup>(25)</sup> (1865) that the cells of the adrenal medulla possess a peculiar staining reaction after fixation with chromium

salts. Similar cells were also found outside the adrenals especially in the abdominal sympathetic. Kohn(22) created the term "chromaffin bodies" for all such cells in and outside of the adrenals and later conceived the term "paraganglia" for such cell accumulations. The number of these paraganglia, or the places where chromaffin cells are found, has been constantly increasing and the boundaries of the chromaffin system are proportionately extended. Thus, they have been found in the inferior mesenteric ganglia (Zuckerlandl's organ), carotid gland, coccygeal gland, ovary, testis, interventricular septum, aberrant adrenals, and in fact wherever sympathetic nerves are present. The chromaffin of the medullary cells has been found identical with adrenalin, the active substance of the adrenal secretion.

The importance of these findings was emphasized when Wiesel(26) in 1903 propounded the theory that Addison's disease was due to a disease of this chromaffin system and perhaps the adrenal, perhaps the extra-adrenal portions of the system were affected in a given case.

Changes in the sympathetic system had already been described in Addison's disease, and pigmentation of the ganglion cells had been mentioned by Wahneau(27) and Babes and Kalindero(28) among others, but it remained for Wiesel to correlate these findings.

From a careful and minute study of the adrenals and the entire sympathetic system in 5 cases of Addison's disease, all of which had caseous adrenals, the latter investigator propounded his theory. He found changes in the sympathetic nervous system similar to those which had been described by many previous authors, that is, proliferation of the connective tissue of the interstices of nerves, thickening of the walls of the blood vessels, atrophy of the ganglion cells and the formation of pigment and lipochrome in them. However, these he considered as not characteristic of Addison's disease, but rather a purely degenerative process such as occurs with age. He created the term "chromaffin system" to indicate those places where chromaffin cells are found and indicated that this includes the sympathetic nervous system and the adrenal medulla. Addison's disease he conceives as a disease of this chromaffin system which may be attacked at any part either in the sympathetic system or in the adrenal medulla. It consists of a progressive atrophy of chromaffin tissue which, as the chromaffin tissue of the adrenal medulla takes part in this degenerative process, spreads secondarily to the cortex. In order that symptoms of the disease may occur, some considerable portion of the chromaffin system must be affected without regard to the exact location; it is not absolutely necessary for the adrenal gland to be among the diseased structures, and disease of one portion may be compensated for by hypertrophy of others. He does not attempt to say how many of the clinical symptoms are attributable to the involvement of the adrenal cortex and admits that pigmentation of the skin is not accounted for.

Karakascheff's(4) conclusions are in direct antagonism to those of Wiesel.

In 1904 the former reported 2 cases and quoted 3 others with total atrophy of the adrenal cortex and from his findings concluded that the cortex especially is of importance in Addison's disease, and causes the whole symptom-complex. Microscopically, he found the cortex almost completely destroyed and the medulla intact. In his own two cases the celiac plexus was normal. He reported one case of a child 5 months old with an old hæmorrhage into the medulla as evidence that the medulla can be completely destroyed without producing Addison's disease. He also quotes Marchand's(11) case, in which there was extensive disease of the solar plexus and upper cervical ganglion without Addison's disease and 6 cases of v. Kahlden's(19) in which the adrenal medulla was caseous and the celiac plexus in great part destroyed, without Addison's disease, as

evidence that the sympathetic system is not responsible. He also refers to 6 cases of Addison's disease reported by Simmonds(13) with adrenal destruction, four of which had normal coeliac plexuses.

Bittorf(6) in 1908 rejected Wiesel's theory and championed the pure adrenal theory contending that disease of the sympathetic system can neither cause Addison's disease nor essentially influence the symptoms. Those cases recorded in the literature as clinically certain cases of Addison's disease without adrenal disease he ascribed to inexact anatomical investigation, and those of adrenal destruction without clinical symptoms he would not recognize. He draws attention to the fact, as did v. Neusser, that lack of pigmentation of the skin does not preclude the possibility of Addison's disease and thinks this may account for the failure to make the diagnosis in some cases. According to Bittorf melano-derma and sympathetic changes are the result of adrenal changes, and he mentions the large and richly pigmented adrenals that occur in negros.

Wiesel considers the cortex and the medulla of the adrenal as two separate organs related only topographically, and believes that the function of the cortex is unknown. Bittorf, on the other hand, conceives the mutual physiological interdependence of the two parts and the unity of the organ. According to Bittorf, muscle poisons, and perhaps other similar metabolic products, reach the cortex of the adrenal through its vessels, and there through simple splitting are deprived of their poison; through a further chemical action in the medulla they are converted into the active substance.

So at the present day the two opposite views are held. The "adrenalists" concede that the changes in the chromaffin system may be present but regard them as secondary or accidental. Those who claim the causative lesions are in the chromaffin system admit that the adrenal medulla may be the initial seat of the disease, but only in so far as it constitutes a part of the system does it produce symptoms.

Another factor, the importance of which is as yet unknown, is introduced in the frequently noted association of Addison's disease with *status lymphaticus*. Averbek(29) noted the condition of lymphatic hyperplasia in his cases of Addison's disease and considered it an essential part of the disease. Star was the first to note persistence of the thymus in Addison's disease, and since then the association of the two diseases has been especially emphasized by Hart,(30) Hedinger,(31) Wiesel,(20) Bittorf,(6) Kahn,(32) and Schridde.(33) Hedinger found *status lymphaticus* in 7 out of 15 cases of Addison's disease. He considers the possibility of their being due to a common cause which is to be found in an imperfect *Anlage* or in an alteration of the chromaffin system, this latter being suggested by Wiesel's observation of a case of *status lymphaticus* with marked hypoplasia of the chromaffin system. Kahn suggests the possibility of the lymphoid hyperplasia being an evidence of reaction to the toxins of Addison's disease. Wiesel in his case just mentioned attributed the sudden death to the hypoplasia of the chromaffin system rather than to the *status lymphaticus*. It is now well known that sudden death is a frequent occurrence in *status lymphaticus* and that many of these cases have a large thymus gland. These ideas are expressed in the terms "thymus death" and "*status thymo-lymphaticus*."

Schridde(34) has suggested that death may be due to a kind of endogenous poisoning through excessive or disordered function of the thymus. Warthin(35) especially has considered that the thymus causes death mechanically by tracheal compression, particularly in children. That the thymus in *status lymphaticus* presents no especial features other than that of delayed resolution or sometimes

slight hyperplasia has been shown by Pappenheimer.(36) This delayed resolution brings the weight of the thymus above that of the normal, which latter, within the last few years, has been shown to differ from all previous conceptions. Hammar,(37) Norris,(38) and Pappenheimer(36) have shown that the weight of the thymus increases up to the 15th year and then the gland undergoes involution. Delayed involution occurs from several causes.

Disease of other glands of internal secretion is not infrequently associated with status lymphaticus, the most noteworthy instance being Basedow's disease. In fact a hypoplasia of the genital organs is claimed by some as an almost constant feature of status lymphaticus.

The insufficiency of our knowledge of Addison's disease is very apparent from a consideration of the conflicting theories just discussed. Hence, the following cases are reported with the idea of furnishing data which may be of value in arriving at its correct interpretation.

#### REPORT OF CASES.

The present writer had the opportunity of studying two cases of Addison's disease during his service in the Pathological Laboratory of Bellevue Hospital, and has recently encountered two instances of adrenal tuberculosis in Filipinos in Manila.

The first case, number 2142, was that of an Italian married woman, 39 years of age, a shopworker, who was under observation only 48 hours before death. The history was that of good health until 3 months previous to admission to the hospital. She then had severe pain in the abdomen and back, which for a time became less severe, and was accompanied by insomnia and loss of appetite and strength. After 2 months her weakness became so marked as to confine her to bed, and she suffered from abdominal pain, vomiting, hiccough, insomnia, constipation, and headache. During the last 3 months of her life she lost 30 pounds in weight and her face and hands grew darker during the last month.

While under observation the essential clinical features were pigmentation (described below), marked asthenia, weak pulse (84 millimeters of mercury), and signs of apical tuberculosis. There occurred an ante-mortem rise of temperature to 104°.2 F. (40°.1 C.) and an attack of pulmonary œdema ended fatally.

The autopsy, which was performed 13 hours after death, was limited to an abdominal incision, through which, however, it was possible to remove the thoracic viscera.

#### PROTOCOL 2142.

The body is that of a well-formed, fairly well-nourished white female of short stature, 39 years of age. Rigor mortis is marked, and there is considerable post-mortem suggillation over the dependent parts. There is no œdema of the skin. The face and back of the hands, the lips, and the gums show brownish pigmentation. The chest is well developed and well formed. The nipples and areolæ are extremely small and black. The waist is narrow. The thighs are well arched laterally, the arching starting from the waist line; anterior arching is not marked. Thighs and legs have a few long hairs. The pubic hair is well developed. There is abundant lanugo over the abdomen. There are hairs over the upper arms, moderate in amount. The hair of the head is abundant and dark. The eyebrows are well developed. There is hair on the nose between the eyebrows, a fairly well developed moustache and long hairs on the chin. There is a moderate

amount of golden-yellow subcutaneous fat. The peritoneum is slightly thickened. The great omentum is long and thin, with a small amount of fat and is adherent to the dome of the bladder and to the anterior abdominal wall. The intestines are collapsed; the serosa is clear, pale, and glistening. The mesentery contains a moderate amount of fat, with a few very pale lymph nodes about 1 centimeter in diameter. The liver reaches the right costal margin and is firmly adherent to the diaphragm. The diaphragm reaches 4th interspace on the right and 5th on the left.

*Lungs.*—There is no fluid in the pleural sacs. The lungs are firmly adherent to the parietes throughout, and each shows fibrocaseous areas near the apex, the remaining lung substance being crepitant and soft, with a smooth surface. The pleurae show a few punctate hæmorrhages. Bronchi and vessels are in good condition. The lymph nodes at the hilus are enlarged and anthracotic, and one or two show fibrous foci.

*Thymus.*—Not discovered owing to the method of section.

*Thyroid.*—The thyroid is slightly enlarged, weighing 35 grams. On section it is more pale than normal, but shows definite glandular structure, apparently with a small amount of colloid.

*Heart.*—The pericardium is firmly adherent to the heart, which is small, without hypertrophy of either ventricle. Endocardium is intact, except for slight pallor and thickening of the mitral valve. The heart muscle is very brown and rather soft. The coronary arteries are in good condition. The aorta shows some fatty degeneration of the intima, especially about the isthmus.

*Spleen.*—The spleen is of about normal size, weighing 150 grams. It is of good consistence and the capsule is thin and smooth. The cut surface is smooth and dark red. The Malpighian bodies are easily visible.

*Adrenals.*—The left adrenal is small and very firm, and on section none of the normal markings of the gland can be distinguished, the gland substance being completely replaced by large, white, partly caseous, masses.

The right adrenal is considerably enlarged, its surface being pale and nodular. On section there are seen few of the markings of the gland, the cortex being represented by faint yellowish streaks. At the lower pole is a large caseous focus, and surrounding the entire cortex, for a width greater than that of the normal gland, is a pale, firm tissue containing a few caseous foci.

*Kidneys.*—The kidneys are of normal size with thin capsules which strip easily from smooth pale surfaces. The two kidneys together weigh 275 grams. On section the consistence is diminished, the cortex is broad and pale, with somewhat injected Malpighian bodies. The pyramids are of a deep blue color. The pelves, ureters, and urinary bladder are free. *Uterus.*—The uterus is small, firm and pale. The endometrium is intact. A mucous plug extrudes from external os. *The Vagina.*—Is normal. *The Fallopian tubes.*—Both are considerably distorted, folded on themselves and adherent, the left being adherent to the anterior wall of the uterus. They are also adherent to the ovaries, which are small, firm, pale, and sclerotic, with a few small cysts. Hanging on the broad ligament at the fimbriated extremity on each side are small unilocular cysts containing a dark fluid.

*Stomach and intestines.*—Contain a considerable amount of pea-green, fluid material, but no formed fæces. Duodenum and stomach show, on their mucous surfaces, numerous rather closely packed but still discrete small pale elevations.

*Liver and gall bladder.*—The liver weighs 1,500 grams and is slightly diminished in size. The capsule is somewhat thickened where adherent to the diaphragm. On section the consistence is somewhat diminished, and the cut surface is dark brown in color, showing the lobules but indistinctly. *Bile ducts.* Normal,

*Gall bladder*.—Contains a considerable amount of dark bile with yellowish sand-like matter suspended in it. Its mucosa is apparently normal.

*Pancreas*.—The duct of Wirsung is normal. The pancreas is small, narrow, flat and pale, and weighs 75 grams. There are numerous enlarged and caseous retroperitoneal lymph nodes.

The gross anatomical diagnosis was: Chronic fibro-caseous tuberculosis of both adrenals; melanoderma; chronic adhesive pleurisy and pericarditis; healed apical pulmonary tuberculosis; healed tuberculosis of bronchial and retroperitoneal lymph nodes; lymphoid hyperplasia of stomach and intestines; chronic parenchymatous nephritis; chronic salpingitis and oöphoritis; status lymphaticus. No accessory adrenals were found. The thymus could not be isolated on account of the method of section.

Microscopically the adrenals showed complete destruction, being entirely replaced by a central caseous area surrounded by tuberculous granulation tissue containing some miliary tubercles and areas filled with plasma cells. The thyroid showed microscopic tubercles as did the liver and spleen. The pancreas showed a marked hypertrophy of the islands of Langerhans. The semilunar ganglia, which were the only parts of the sympathetic system preserved, contained chromaffin.

The investigation of the chromaffin system in this case was limited to the adrenals and semilunar ganglia, in the former of which it was entirely lacking. Thus far this case might well accord with either Wiesel's or Karakascheff's theory and forms alone an insufficient field for theorizing as to the pathogenesis of the disease. However, the simultaneous lesions in the adrenals, thyroid, and pancreas, form apparent histological evidence of what has been shown experimentally in other connections. Eppinger, Falta, and Rudinger<sup>(39)</sup> have shown that both adrenals and thyroid inhibit the pancreas, and Falta<sup>(40)</sup> has reported one case in which after thyroidectomy an undoubted hypertrophy of the islands of Langerhans occurred. In our case there was complete suppression of adrenal function and in all probability dysthyroidism can be postulated in view of the thyroid tuberculosis. This would remove normal inhibition from the pancreas and lead to the hypertrophy of the islands of Langerhans, which is supposedly histological evidence of hyperfunction.

The second case, number 2262, was that of a Canadian farmer, 34 years of age, who at 3 years of age had a lesion of the left hip joint which resulted in complete ankylosis. He had had bronzing of the skin for 11 years, and had lost 25 pounds in weight in the 3 months previous to his entrance to the hospital, where he sought admission on account of weakness, soreness of the muscles, and loss of appetite. Aside from his ankylosed hip, pigmentation, asthenia, soreness of the muscles and low blood pressure (85 millimeters of mercury) he presented no noteworthy clinical symptoms.

#### PROTOCOL 2262.

The body is that of a well built and muscular adult white male of about 35 years. The left lower extremity is 6 to 8 centimeters shorter than the right and is flexed and adducted. Rigor mortis persists, but is disappearing in toes and fingers. The left leg can not be rotated, apparently being fixed at the hip, and is considerably less in circumference than the right at both thigh and calf. The



skin of the head, especially that of the forehead, is a very dark brown, resembling sunburn, this being less marked over the face and neck. The skin of the trunk and abdomen is dirty yellowish in color. The dorsum of both hands is deep brown in tint, as if sunburnt. Over both extremities and trunk in front and behind are numerous symmetrically distributed lesions, all being about 7 millimeters in diameter, round, macular, with a narrow, dark brown pigmented rim, and a whitish, smooth central portion, not elevated above the surface and not scaly. In a few of the maculæ the central portions are slightly depressed. The inner portions of the lips and mucous membranes of the mouth show a few black pigmented areas. On the skin of the penis and glans are several dark bluish pigmented areas of small size (2 or 3 millimeters).

The hair of the scalp is of good growth, brownish, lustrous. The beard and moustache are scant. The axillary hair is scant, the individual hairs long. There are a few long black hairs around the nipples, scant short hair on the trunk, a few also on lineæ of abdomen, and moderate pubæ. The hair on the thighs and lower legs is poorly developed. The anus and perineum have a good growth of hair. There are no lesions around the anus. No mucous patches are visible.

There is no œdema of the subcutaneous tissues.

The head is moderately round in type. The pubic hair is feminine in type. The superficial lymph nodes are not palpable.

On section there is a small amount of panniculus abdominis. The musculature is everywhere well developed. The abdominal cavity is free from fluid and adhesions. The liver reaches the costal margin. The diaphragm is at 4th rib on the right and 4th space on the left. The costal cartilages are not ossified.

*Lungs*.—The left lung is everywhere adherent; the right everywhere free. Right pleura is filled with a clear straw-colored fluid. The left lung is everywhere well aerated and dry; it is slightly congested. The right lung, except for apical thickening of the pleura, resembles the left. The bronchial lymph nodes are small and anthracotic. There are no signs of tuberculosis in the nodes or in the lungs. The bronchi are congested, otherwise normal.

*Thymus*.—Persistent. It is red and fleshy, and in places well developed. It extends to the auricle over the pericardium where it is thin. It weighs 21.5 grams.

*Heart*.—The pericardial sac is not distended; it contains 20 cubic centimeters of clear fluid. The epicardial fat is moderate in amount, being excessive at the apex. There is no distension of the cavities, which contain chicken-fat clot, especially on the right side. All the valves are normal except the mitral which is thickened at the margins. The anterior papillary muscles of the mitral are short and thick at the apex; chordæ tendinæ are short. The apices of the papillary muscles are pale and thickened. The aorta is normal as to thickness and elasticity, the abdominal portion shows above the bifurcation a whitish, raised patch. The iliacs normal. The aorta measures 75 millimeters above the cusps, 45 millimeters at the celiac axis, and 35 millimeters at its bifurcation.

*Spleen*.—Normal in size and appearance.

*Adrenals*.—The left adrenal measures 55 by 22 by 12 millimeters and weighs 6.5 grams. It retains its original contour. On section it is seen to be apparently completely replaced by a pale yellowish caseous mass, and there is no vestige of glandular tissue visible. At the anterior extremity the vessels of the medulla can be seen. The right measures 65 by 30 by 13 millimeters and weighs 12 grams. It also retains its contour and is replaced by a yellowish caseous material, which extends to the capsule. At its lower and posterior extremity

the medullary vessels are visible with perhaps a small amount of cortical substance at the periphery.

*Semilunar ganglia.*—On the two sides considerably larger than normal, but very flat and rather firm in consistence.

*Kidneys.*—The kidneys are embedded in a small amount of perinephric fat, and are of about normal size with thin capsules which strip easily from pale surfaces. On section they are of diminished consistence (owing to post-mortem changes). The cortex is of normal width, rather pale with irregular red striations. The pyramids are also rather pale. The pelves and ureters are free.

*Urinary bladder.*—Contracted and empty. A few ecchymoses on the posterior wall.

*Intestines.*—The lower half of the small intestine shows many raised hypertrophic lymphoid follicles. All the Peyer's patches are raised, and hyperplastic, and are occupied by a follicular, stippled mass of tissue. Some of the Peyer's patches show mottled greenish and black pigmentation. The large intestine in its lower portion contains a fairly solid mass of fæces. The follicles are everywhere numerous, prominent and flat, with pigmented borders. The mesentery contains a moderate amount of fat.

*Stomach.*—Normal in size, without distension. Its mucosa is clean and covered with mucus. No lymphoid hyperplasia is visible.

*Liver.*—Normal in size. The capsule is smooth. The organ is dark brown in color. Section shows a normal appearance with rather indistinct markings. The gall bladder is normal, and slightly distended. The portal vessels are normal. The bile duct is patent.

*Pancreas.*—Pinkish in color. Normal in size and lobulations. It measures 160 millimeters in length, 12 millimeters in average thickness, the head being 45 millimeters wide and the tail 30 millimeters and weighs 65 grams.

*Neck organs.*—Tongue is large, papillæ at base being prominent. The lingual tonsils are very large. The pharyngeal tonsils are enlarged irregularly and indurated. The lymphoid tissue of the pharynx and larynx is hypertrophic. There is a slight laryngeal œdema. The trachea is normal. The œsophagus in its lower portion shows several raised, whitish, linear patches.

*Thyroid.*—Rather large. On section it shows normal colloid appearance. It weighs 45 grams, each lateral lobe being 50 by 30 by 20 millimeters and the isthmus proportionate in size.

The parathyroids are small.

*Lymph nodes.*—The cervical and axillary lymph nodes are small and pale. The mesenteric lymph nodes are very small and pale, except for one rather large one (about 1 centimeter in diameter). There are some flat nodes in the ileo-cæcal chain.

*Brain.*—The skull and scalp are normal. The dura is normal. The pia shows no œdema. The vessels at base are normal. The ventricles and ependyma are normal. Section of brain substance reveals no gross lesion. Ears normal. The pituitary is normal in size.

After excision of the hip joint, a transverse section through the trochanter and head of the femur and the acetabulum shows the neck of the femur considerably shortened, and the head of the bone firmly fixed in the acetabular cavity, so that the outline of the margin between the femur and the acetabulum is very indistinct. About this line there is a considerable amount of firm, white, bone tissue. The marrow of the head shows one area of complete destruction about 2 centimeters in diameter. The marrow is replaced by fibrous tissue in some places, and in others is destroyed and replaced by a yellowish-white substance which is softer than the bone.

The gross anatomical diagnosis was: Caseous tuberculosis of the adrenal glands; chronic coxitis (tuberculous?); chronic adhesive pleurisy; chronic ossifying myositis of left gluteus medius; hyperplasia of lymphoid tissue of lingual and faucial tonsils, pharynx, larynx, spleen, small and large intestine; congestion of lungs; status lymphaticus. No accessory adrenals were found and there was no arterial hypoplasia.

Microscopically, the adrenals showed the same complete fibro-caseous destruction with only small vestiges of the cortex at one part. The semilunar ganglia contained chromaffin. There were some small cervical nodes which contained healed tuberculous areas. The pancreas and thyroid showed no marked pathological changes. One parathyroid which was sectioned was found to be the seat of a very extensive fibrosis, showing only small remnants of the gland embedded in the fibrous mass. The thymus gland showed marked hyperplasia.

Extracts of the adrenal masses were made according to the method described by Wells and Greer,<sup>(41)</sup> and the intravenous injection of 2 cubic centimeters produced no rise of blood pressure in the rabbit. The extract of a normal adrenal, obtained the same length of time after death and prepared in exactly the same way, produced a distinct, sharp rise when 0.5 cubic centimeter was injected. In order to eliminate a possible counteracting depressor action of any of the products of caseation, an extract of caseous mesenteric glands from a tuberculous infant was injected intravenously and no change in blood pressure was observed.<sup>1</sup>

Similarly, the extract of the caseous adrenals gave a negative Ehrmann's reaction; that is, it produced no dilatation of an excised frog's eye in several hours, while the extract of the normal adrenal produced temporary dilatation, as did also adrenalin chloride in 1 in 10,000 solution. These tests were performed with naked-eye readings simultaneously under identical conditions of temperature and light, and the independent readings of four observers coincided. This is mentioned because Schultze<sup>(42)</sup> has devised an elaborate apparatus for observing the pupil and making accurate measurements under constant light and temperature and considers naked-eye readings of no value. Oliver and Schaeffer<sup>(43)</sup> who were the first to describe the angiotonic effect of adrenal extract on intravenous injection, have also found the extracts of the adrenals in two cases of Addison's disease inactive as far as the blood-pressure-raising reaction was concerned.

The salient features of this second case, then, were prolonged bronzing of the skin, with acute symptoms of Addison's disease lasting 3 months,

<sup>1</sup>Since writing this there has come to hand an article by Clyde Brooks in *Journ. Exp. Med.* (1911), 14, 550, on the Absence of Adrenalin in Malignant Renal Hypernephromas. In this he reports negative physiological tests for adrenalin in (A) Metastatic tissue from an adrenal tumour,

(B) Two typical hypernephromas,

(C) Blood from patient with malignant hypernephroma. In his report of the literature he omitted the report of my tests which was published in *Trans. N. Y. Path. Soc.* (1909), N. S. 9, 80.

adrenal tuberculosis without other tuberculous foci except those long healed, parathyroid fibrosis, and status lymphaticus. It is worthy of note that adrenal tuberculosis may occur without other active or recognizable tuberculous foci. It is also true that severe loss of weight may occur on account of adrenal tuberculosis without other widespread tuberculous lesions. This patient lost 25 pounds in 3 months. This case, like the first, showed a status lymphaticus and destruction of another endocrine gland.

The two cases of tuberculosis of the adrenals which the writer has had the opportunity of studying in Manila were accidental autopsy findings in which the clinical diagnosis was generalized tuberculosis. Both of these occurred in Filipinos, thus raising the question as to the possibility of making the clinical diagnosis of Addison's disease in dark races. Bittorf and Neusser state that melanoderma is not a necessary integral part of Addison's disease, but agree that it is of very great diagnostic importance. In these cases no excessive pigmentation of the mucous membranes or of the skin could be observed on very close examination on the autopsy table, aside from two isolated dark spots on the tip of the tongue of the second case. It was considered at the time that these might have occurred from extraneous sources, such as the teeth, and microscopical examination was of little assistance, since the pigment involved not only the epithelium but the corium as well, and might have reached the part from either direction.

The first case, number 1350, was a male Filipino, 26 years of age, who had been imprisoned for 7 years and had been in the tuberculosis ward of the hospital for 3 years. From May, 1906, until April 15, 1908, when he was transferred to the tuberculosis ward, various diagnoses were made at different times and these diagnoses constitute the only available record during that period. These were, acute dyspepsia, acute articular rheumatism, malaise, acute bronchitis, neurosis (anæsthesia of the right arm), intestinal colic and conjunctivitis. In 1907 amœbæ and ova of *Trichuris trichiura* were found in his fæces, but disappeared after treatment. The urine was negative. Tubercle bacilli were found in the sputum for the first time in April, 1908. At autopsy he was found to be a much emaciated Filipino who showed no excessive pigmentation of his mucous membranes. The skin being normally of a uniform, dark color, no pathological bronzing could be determined. The anatomical diagnosis made at the autopsy was: Chronic ulcerative pulmonary tuberculosis (very extensive); chronic adhesive pleurisy, tuberculous; chronic bronchitis; tuberculous colitis; congestion and parenchymatous degeneration of the liver; parenchymatous degeneration of the heart and kidneys; tuberculous lymphadenitis of the bronchial and cervical nodes; tuberculosis of adrenals.

The pulmonary tuberculosis was very extensive, practically all lung tissue being destroyed.

The left adrenal weighed 5 grams and it showed on the surface smaller and larger foci, the largest measuring as much as 1 centimeter in diameter. On section these foci were firm, pale, circumscribed, and occurred mostly in the cortex of the gland, although some extended through the cortex to the medulla; otherwise the adrenal tissue had a normal appearance. The right adrenal weighed 4.5

grams and presented a similar appearance. The spleen weighed 210 grams, pancreas 90 grams, thyroid 9.3 grams, and the testes 9.5 and 10 grams respectively. The spleen showed some interstitial splenitis, but the rest of these organs the weight of which is given showed no change. The weights of these viscera form about the average of the weights of the organs in the tuberculous cases without adrenal involvement.

There was no evidence of status lymphaticus in this case and the thymus was embedded in such a mass of mediastinal adhesions that it was not isolated. The microscopic examination of the adrenals confirmed the gross anatomical diagnosis. Extensive caseation of the cortex of the adrenal occasionally involving small parts of the medulla constitutes the main lesion. The caseous areas are surrounded by zones of small round cells *without* fibrosis. This lack of reactive connective tissue is quite uniform throughout this case, and indeed appears characteristic of the tuberculous lesions as encountered in Filipinos. The cortex is not all destroyed, and that which remains shows a nodular hyperplasia and dilatation of the capillaries. The individual cells, except where compressed by the tubercles, show the normal structure; the protoplasm stains rather poorly with eosin and is reticulated; the nuclei contain abundant chromatin and occasionally assume giant forms. The inner zone of the cortex contains abundant native pigment (not chromaffin). The medulla shows areas of coagulation necrosis even where not directly the seat of tuberculosis, with pyknosis of the nuclei and even complete nuclear destruction. Chromaffin is very scant. The semilunar ganglia contain chromaffin.

The second case, number 1352, is that of a 57-year old Filipino who had been in prison 2.5 years. In 1909, two years before his death, he had a "tuberculous abscess of the scrotum." One week before death he was admitted to the hospital on account of general weakness. His weakness was extreme and for 2 days previous to death he was practically pulseless. Aside from the evidence of the old scrotal abscess, there were but few symptoms on which to base a diagnosis.

Dr. J. W. Smith, under whose charge the patient was, made the diagnosis of generalized tuberculosis in spite of the lack of definite physical signs and the absence of tubercle bacilli from the sputum.

At autopsy the only evidence of excessive pigmentation consisted in 2 small, dark areas on the sides of the tongue. He was extensively emaciated. The gross anatomical diagnosis was: Chronic miliary pulmonary tuberculosis; emphysema of the lungs; chronic adhesive pleurisy; tuberculous enteritis; parenchymatous degeneration of the heart, liver, and kidneys; chronic perisplenitis; tuberculosis of both adrenals, the right kidney, prostate gland, left epididymis, right testicle, and spermatic cords.

The left adrenal measures 6 by 1.5 by 1 centimeter and weighs 4.1 grams. It is pale and on section presents numerous smaller and larger conglomerate caseous foci. The normal architecture of the gland is completely obliterated so that no adrenal tissue can be recognized. The right adrenal measures 5.5 by 3 by 2 centimeters and weighs 10.7 grams. This is also distorted in shape and the seat of one large nodule (2 by 2 by 1.5 centimeters) and several smaller ones, so that only a small vestige of the gland can be recognized situated at the lower pole. These nodules are pale, fairly firm, with yellow striæ traversing them. The spleen weighs 120 grams, testes 9.3 and 8.2 grams, pancreas 54 grams, and thyroid 7.3 grams. The weights of adrenals and testes are increased on account of tuberculosis. Microscopically, no vestige of medullary tissue is found in the adrenals. There are islands of intact cortical cells and many islands of these cells surrounded by and included in the tuberculous tissue in all stages of degeneration and necrosis. The capsule is thickened and there is a small amount

of granulation tissue beneath it which includes many vessels which are the seat of a very marked endarteritis and periarteritis. The proliferated adventitia of the vessels frequently contain numerous tuberculous giant cells. Plasma cells are numerous. Chromaffin tissue is present in the cells of the semilunar ganglia in small amount.

These two cases occurred in the hospital at Bilibid Prison where there is a large number of patients under the care of one physician, and these cases did not attract enough attention to make them the subject of any elaborate physical examination.

The writer is inclined to believe that the first case was a simple case of adrenal tuberculosis without Addison's disease. However, the second case is more probably one of Addison's disease. The extreme prostration of the patient and the low blood pressure during the last week might possibly have been accounted for by his widespread tuberculosis, but the fact that he was able to be at work until a week before his death would seem to point to some more definite anatomical feature which could account for a lack of some necessary tonic secretion. In this case especially the anatomical evidence is that the adrenals had been functionless for a considerable time and the final prostration would more plausibly be accounted for by the eventual failure of other tissues to carry on the vicarious function of the adrenal. This appears to me to be a very strong point in favor of viewing the adrenals as one part of a system, the complete destruction of which may for a time be compensated for by other parts of the system. Whether this system be the adrenal medulla and the sympathetic nervous system, or the adrenal cortex and some other gland which may act vicariously for it, is not proved by my experience.

#### SUMMARY.

1. Two clinically certain cases of Addison's diseases have been described in which the adrenals were destroyed by tuberculosis and the semilunar ganglia contained chromaffin. In both of these, other endosecretory glands were the seat of pathologic processes. In one, hyperplasia of the islands of Langerhans was associated with adrenal and thyroid tuberculosis; in the other, one parathyroid was cirrhotic.

2. A case of adrenal tuberculosis without changes in the semilunar ganglia and without recognized Addison's disease occurred in a Filipino.

3. A second case in a Filipino with adrenal tuberculosis and intact semilunar ganglia was probably one of Addison's disease.

The difficulty of diagnosing Addison's disease in dark-skinned races is great on account of the absence of pathological melanoderma and the possible presence of wide spread tuberculosis. If Addison's disease does occur in dark-skinned races it substantiates the opinion that melanoderma is not an essential feature of the disease, while it emphasizes its importance as a diagnostic sign.

4. The adrenals from one case of Addison's disease contained no adrenalin estimable by the angiotonic and pupil-dilating reactions.

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# RICE AS FOOD: INVESTIGATION OF THE NITROGEN AND PHOSPHORUS METABOLISM ON A DIET CONSISTING PRINCIPALLY OF RICE AND OTHER VEGETABLE FOODSTUFFS.

BY HANS ARON and FELIX HOCSON.

(From the Department of Physiology, College of Medicine and Surgery, University of the Philippines.)

## INTRODUCTION.

Rice is probably the most prominent vegetable food of man. A rough estimate shows that in Asia alone at least 400 million Indians, Chinese, Japanese, and Malays consume rice. Only a small quantity of other food is eaten by the lower classes of these people, because their low earning power does not permit a richer diet. The question has been considered frequently whether such a diet is a sufficient one, and it gains further importance because of the close connection which has been proved to exist between the consumption of certain classes of rice and the existence of those polyneuritic diseases which are commonly termed beriberi.

The variations in the composition of the different varieties of rice are not so great but that from our standpoint we can speak of rice in general. However, the different methods of treatment and milling alter considerably the composition of the grain, as has been pointed out in a previous paper.<sup>1</sup>

We have determined the phosphorus content of 28 different classes of rice during the past two years. The following table shows plainly that the phosphorus content within narrow limits is determined by the grade of milling. The whiter the rice the poorer it is in phosphorus.

<sup>1</sup> *This Journal*, Sec. B (1910), 5, 81-98.

TABLE I.—Composition of various classes of rice milled in different ways.

Num- ber of sam- ple.	Variety of rice.	Appearance.	P <sub>2</sub> O <sub>5</sub> .	Nitrogen.	H <sub>2</sub> O.
			<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>
1	Liverpool	Very white	0.15	1.07	11.67
2	Valenciana	do	0.20		
3	Metabolism experiment, May, 1910.	Pure white. Trade-mark "Ia, Blanco."  White	0.28	1.29	11.75
4	Metabolism experiment, January, 1910.		0.28	1.32	
5	Laguna, Ia Blanco		0.31		
6	Ilocano "Sup. Blanco"		0.32	1.20	
7	Metabolism experiment, 4 ff		0.32	1.06	
8	Culion, December, 1908		0.32		
9	Manila Market		0.33		
10	Metabolism experiment, January, 1910.		0.33	1.48	
11	Macán machinery rice		0.34		
12	Metabolism experiment, 5	Quite white slightly yellow- ish.	0.37	1.23	
13	Bombay	Brownish, pericarp incom- pletely removed.	0.41	1.25	11.97
14	Cape Engaño	Slightly brownish, pericarp partly removed.	0.43		
15	Tagalog D	Slightly brownish, pericarp partly removed.	0.45	1.42	
16	Calcutta	Brownish, pericarp incom- pletely removed.	0.45	1.24	11.63
17	Culion, January, 1910		0.46		
18	Macán, Native Mill		0.46		
19	Siam, Asylum		0.52		
20	Tagalog C	Brownish, greater part of pericarp not removed.	0.53	1.43	
21	Laguna, slightly milled		0.56		
22	Metabolism experiment, January, 1910.		0.57	1.19	
23	Tonkin		0.58		
24	Ilocano 4		0.58		
25	Culion, October, 1910		0.60	1.19	
26	Tagalog Pinawa		0.73	1.54	
27	Ilocano Pinawa		0.75	1.27	
28	Pinawa, Metabolism experi- ment, 3.	Husked only and cleaned of husk by air blast.	0.77	1.29	

TABLE II.—Descriptions of rice samples.

Sample number.	Treatment.	Phospho- ric acid anhy- dride.	Protein. (nitrogen x 66.25 per cent.)	Weight in 1,000 grams.	Removed by mill- ing.
		<i>Per cent.</i>			<i>Per cent.</i>
Iloca- no rice.	1 Husked only, "Pinawa"	0.77	7.94	23.69	
	3 Larger distance between cones than is usual: undermilled	0.58		22.55	4.8
	5 Superior Blanco; overmilled	0.32	7.50	20.52	13.4
Tagal- og rice.	A Husked only, "Pinawa"	0.73	9.63		
	C One polisher, one cone, regular distance; Ila Blanco	0.53	8.96		
	D Two polishers, two cones regular distance, grains partially broken	0.44	8.90		

The nitrogen content of rice differs considerably less than the phosphorus content, but the more intensively a given rice is milled the poorer it becomes in nitrogen; however, the nitrogen content of different classes of rice varies so greatly that this figure, in any particular case, gives no indication of what treatment the grain had been subjected to in milling. For practical purposes, we can distinguish three stages of milling if we judge by the phosphorus content of the rice. These are: (1), rice, husked only, 0.7–0.8 per cent phosphoric anhydride; (2), undermilled rice, 0.45 to 0.6 per cent phosphoric anhydride; (3), overmilled rice, 0.15 to 0.35 per cent phosphoric anhydride.

Rice as food, has the following characteristics: (1), it is comparatively poor in protein; (2), it is very rich in carbohydrates, especially in starch; (3), the white variety is low in ash and especially in phosphorus. One hundred grams of rice, representing about 350 calories, contain only 7 to 8 grams of protein. Therefore, the daily demand for energy of some 2,100 to 2,400 calories would be supplied by 600 to 700 grams of rice; on the other hand, this quantity would contain only 45 to 55 grams of protein; and if the grain were white, it would then afford only 1.5 to 2 grams of phosphoric anhydride. In fact, the quantities of the latter constituent which are taken will often be still lower if other foods, rich in carbohydrates or fat, are consumed in addition.

Several authors point out the fact that a diet consisting for the greater part of rice must of necessity be very voluminous. This idea is based on the supposition that the rice-eating native cooks his rice in the same way as the European. Scheube<sup>2</sup> has shown this to be erroneous. Our own observations as well as those of other residents in the Orient prove that the Japanese, Chinese, and Malays cook rice with so little water that, although the grain becomes softened, it remains apparently dry. In carrying on metabolism experiments, we have weighed, twice daily for ten days, rice prepared by natives. This was done before and after cooking, and we found that within narrow limits 100 grams of uncooked rice gives about 250 grams of cooked rice. Rarely is more than 300 grams of rice, which cooked would weigh 750 grams, taken at one meal. This is not a very great amount, especially when we consider that the Malay at least, and, we believe, the Chinese and Japanese also, seldom drink with their meals; the majority of them drink afterward, and even then only small quantities. An average European very frequently drinks as much as one liter of liquid with each meal, so that his meal certainly is a much more voluminous one than that of the rice-eating Oriental.

These considerations induced us to investigate the nitrogen and phosphorus metabolism of people living mainly on rice or on a similar

<sup>2</sup> *Arch. f. Hyg.* (1883) 1, 352–83.

diet more or less deficient in nitrogen and phosphorus. As these questions seemed to us to be of fundamental importance, and as they were emphasized by Schaumann<sup>3</sup> in his last extensive publication, we continued the experiments which were described previously,<sup>4</sup> using prisoners in Bilibid Prison. Our thanks are again due to the authorities of that institution for their kindness. Two medical students<sup>5</sup> also served with great enthusiasm as subjects for further experiments.

The basis of all rations was rice. In addition, we gave varying amounts of vegetable and animal foodstuffs, such as bread, fruits, vegetables, sugar, fish, bacon, and lard. The bread used in a great number of experiments was made of fine wheat-flour, very similar to white rice in its content of nitrogen, phosphorus, and carbohydrates. The arrangement of the experiments was practically the same as described in our previous paper. The subjects were all healthy men. Most of the prisoners had previously undergone small surgical operations, but had fully recovered at the time they volunteered for the experiments. We paid especial attention to securing men free from intestinal disturbances and who had good digestion. Their faeces, in two microscopical examinations, were free from intestinal parasites and eggs. The prisoners were isolated in a shady room of the hospital and did no work during the experiments. An exact control was possible only in this way. At the same time the secretion of sweat could be reduced to a minimum. Both medical students who took part in the experiments lived near the laboratory and performed but little laboratory work during the period of special diet. Therefore, the daily amount of work which our subjects did was extremely limited and the food was comparatively low in caloric value. Experiments conducted during severe muscular work with a corresponding greater intake of food of composition similar to that given in our experiments, are desirable. However, such experiments in the Tropics would be very complicated owing to the necessity of collecting the sweat and determining the nitrogen secreted in it.

Four experiments<sup>6</sup> not open to criticism, have been found by us in the literature. In these, nitrogen metabolism has been determined on a diet consisting mainly of rice. They are compiled in Table III.

So far as we know, phosphorus metabolism on a diet such as that given in Table III hitherto has not been investigated. A summary of our own 15 experiments on 9 normal men is given in Table IV. It shows the quantities of nitrogen and phosphorus taken with the food, the amounts of nitrogen and phosphorus excreted in the urine and faeces, the percentage distribution of nitrogen and phosphorus, and, finally, the nitrogen and phosphorus balance.

<sup>3</sup> *Arch. f. Schiffs- u. Trop.-Hyg., Beiheft* (1910), 14, 13-372.

<sup>4</sup> *Loc. cit.*

<sup>5</sup> Messrs. Velarde and Feliciano.

<sup>6</sup> Max Rübner, *Ztschr. f. Biol.* (1879), 15, 115-202; Karl Thomas, *Arch. f. Anat. u. Phys.* (1909), 219-302; Muneo Kumagawa, *Virchow's Arch.* (1889), 116, 370-431.

TABLE III.

Num-ber.	Author.	Subject.	Body weight.	Daily food.	Dura- tion of exper- iment.	Calories.		Intake—				Out put—				Nitro- gen balance.
						Total.	Per ki- logram body weight.	In rice.	In other food.	Total.	Per ki- logram body weight.	Urine.		Feces.		
												Grams.	Per cent of intake.	Grams.	Per cent of intake.	
1	Rübner (4)	Man 23 years old.	Kilos. 72	<div>638 grams rice</div> <div>24 grams meat extract</div> <div>82 grams bone marrow</div> <div>500 grams rice flour</div> <div>320 grams milk sugar</div> <div>100 grams starch</div> <div>30 grams cane sugar</div> <div>2 lemons and salt</div>	2	2,970	41	8.9	1.55	10.45	0.14	11.59	<100	2.13	20.4	-3.27
2	Thomas (5)	Author	75.9	<div>450 grams rice</div> <div>80 grams miso</div> <div>250 grams turnips</div> <div>10 grams shoyu</div> <div>7 liters tea</div> <div>800 cubic centimeters beer</div>	5	2,030	42	4.46	2.61	7.07	0.15	7.06	99.9	1.66	23.5	-1.65
3	Kumagawa (6).	Author; 27 years old.	48	<div>600 grams rice</div> <div>100 grams miso</div> <div>300 grams turnips</div> <div>10 grams shoyu</div> <div>585 cubic centimeters tea</div> <div>595 cubic centimeters beer</div>	9	2,590	54	6.00	2.76	8.76	0.19	6.07	6.93	2.03	23.2	-0.66

TABLE IV.

Ex- peri- ment num- ber.	Subject.	Body weight.  <i>Kilos.</i>	Daily intake of food.						Dura- tion of exper- iments.	Calories.	
			Rice.	Bread.	Fish.	Sugar.	Bacon.	Coffee.		Other food substances.	Per kilo- gram of body weight.
			<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Grams.</i>	<i>Days.</i>	Daily.	
1	Medical student V	35.7	400			45	60	150	3	2,360	45
2	Medical student F	54.0	400			40	60	175	3	2,400	44
3	Prisoner 20560 (C.)	49.0	400			50	50	300	4	2,200	44
4	do	48.6	400			50	50	300	4	2,200	45
5	Prisoner B	64.0	300	400		100	75	200	4	2,600	41
6	do	64.0	300	400		90	75	400	4	2,600	41
7	do	64.0	300	400		90	75	300	4	2,600	41
8	Medical student F	54.0	400		120	40		175	4	2,100	39
9	Prisoner 4017 (D.)	48.5	200	150	75	150		500	6	1,650	38
10	Prisoner A	52.5	300	300	40	50		300	4	1,880	37
11	do	52.5	250	250	40	100		300	4	1,880	37
12	Prisoner 6917 (E.)	54.0	250	200	100	100		500	3	1,750	31
13	do	54.0	250	200	100	100		500	3	1,750	31
14	Prisoner 18736 (G.)	45.9	200	200	60	50		500	4	1,350	30
15	Prisoner 8110 (H.)	53.0	250	200	60	75		500	4	1,600	30

a Red rice, husked only.

Ex- peri- ment num- ber.	Subject.	Nitrogen—										Phosphoric acid.					
		Intake.				Outgo—						Intake.		Outgo—		Balance of P <sub>2</sub> O <sub>5</sub> .	
		Animal nitro- gen.	Veget- able nitro- gen.	Total.	Per kilo- gram of body weight.	In urine.		In faeces.		Bal- ance of nitro- gen.	Total P <sub>2</sub> O <sub>5</sub>	Per kilo- gram of body weight.	In urine.		In faeces.		Grams.
						Nitro- gen.	Per cent of intake.	Nitro- gen.	Per cent of intake.				P <sub>2</sub> O <sub>5</sub> .	Per cent of intake.	P <sub>2</sub> O <sub>5</sub> .	Per cent of intake.	
1	Medical student V	Grams.	Grams.	Grams.	Grams.	Grams.		Grams.		Grams.	Grams.	Grams.	Grams.		Grams.		Grams.
2	Medical student F	0.49	5.49	5.98	0.11	5.87	98.2	1.77	29.1	-1.66	3.22	0.066	1.03	32.0	2.03	63.1	+0.16 <sup>a</sup>
3	Prisoner 20560 (C.)	0.49	5.60	6.09	0.11	4.86	90.1	2.06	33.3	-0.83	1.42	0.029	1.04	73.2	0.83	58.4	-0.45 <sup>b</sup>
4	do	0.38	5.45	5.83	0.12	4.26	73.1	3.11	—	-1.68	1.50	0.023	1.74	>100	0.73	48.7	-0.97
5	Prisoner B	0.38	4.53	4.91	0.10	4.26	86.7	2.33	—	-4.67	4.91	0.077	1.56	31.7	1.85	37.7	+1.50
6	do	0.31	9.26	9.57	0.15	10.85	>100.0	3.39	35.4	-2.08	1.88	0.029	1.57	83.5	0.61	32.4	-0.30
7	do	0.25	9.16	9.41	0.15	8.26	87.7	3.23	34.3	-1.98	—	—	—	—	—	—	—
8	Medical student F	1.95	9.11	11.06	0.17	9.66	87.3	3.38	30.6	-0.43	—	—	—	—	—	—	—
9	Prisoner 4017 (D.)	4.26	5.66	9.92	0.18	8.20	82.6	2.15	21.7	+0.06	1.28	0.033	0.80	62.5	0.49	38.0	-0.01
10	Prisoner A	2.84	4.76	7.60	0.18	5.90	77.5	1.64	21.6	+0.38	1.57	0.032	1.14	72.6	0.52	33.7	+0.01
11	do	2.52	8.47	10.99	0.21	7.97	72.5	2.64	24.0	+0.57	5.46	0.104	1.38	25.3	3.46	63.4	+0.62
12	Prisoner 6917 (E.)	2.52	8.97	11.49	0.23	7.18	62.5	3.74	—	+0.72	1.77	0.033	1.23	57.6	0.76	42.9	-0.22
13	do	4.37	5.90	10.27	0.19	8.96	87.4	2.03	19.0	-0.73	1.77	0.033	1.11	57.6	0.73	41.2	-0.10
14	Prisoner 18736 (G.)	4.37	5.90	10.27	0.19	8.73	85.1	2.27	22.1	-0.80	1.45	0.032	0.95	65.5	0.58	40.0	-0.08
15	Prisoner 8110 (H.)	2.62	5.28	7.90	0.17	6.72	85.1	1.98	25.1	—	1.63	0.031	1.21	74.2	( <sup>c</sup> )	( <sup>c</sup> )	( <sup>c</sup> )
		2.62	5.90	8.52	0.16	6.87	80.6	( <sup>c</sup> )	( <sup>c</sup> )	—	—	—	—	—	—	—	—

<sup>a</sup> Red rice, husked only.<sup>b</sup> White rice, polished.<sup>c</sup> Limitation of faeces a failure. Figures for urine only.

The detailed records of five of these experiments have already been published in a previous paper<sup>7</sup> (Nos. 5, 6, 7, 10, and 11), while a complete record of the remaining ten will be found at the end of this paper.

#### NITROGEN METABOLISM.

In their experiments with a rice diet, neither Rübner nor Thomas was able to establish nitrogen equilibrium in spite of a comparatively great intake of calories. However, they experimented only with Europeans. The nitrogen excretion likewise exceeded the nitrogen taken with the food in our experiments numbered 1 to 4, made on Malays. Kumagawa succeeded in establishing nitrogen equilibrium in only 1 experiment, in which 8 grams of nitrogen, or 0.19 gram per kilogram and 2,590 calories per kilogram were consumed. However, it must not be forgotten that in addition he ate considerable quantities of turnips and other foodstuffs. (See Table III.) Therefore, in metabolism experiments carried on by our method, it appears to be difficult to give the amount of nitrogen needed by the body by means of a diet of pure rice, with such additions as sugar, bacon, and bananas as are shown in Table IV. It might be easier to give the quantities of protein necessary to establish nitrogen equilibrium if the subjects were performing muscular labor with a resulting greater demand on energy than was the case with our volunteers who practically did no work. A number of experiments on metabolism in which mixed diets of rice and fish, or rice and meat and vegetables, were given, have been performed, but it would take too much space to review all of these.<sup>8</sup> Therefore, we will limit our discussion to experiments numbered 5 to 15 in our series. We employed in these instances varying quantities of nitrogen as well as varying numbers of calories.

To facilitate comparison we have reduced the figures for calories, the nitrogen intake, and the nitrogen balance, to a uniform standard of 50 kilograms of body-weight and these values are given in Table V.

<sup>7</sup> *Loc. cit.*

<sup>8</sup> W. O. Atwater and C. F. Longworthy, *Bull. U. S. Dept. Agr. Off. Exp. Sta.* (1898), No. 45. C. Cijkmann, *Virchow's Arch.* (1893), 131, 147, 180. Taniguti, *Arbeit a. d. kais. jap. militär Med.* Lebraust, 1, 85, 90. *Review Malays Jahresbericht* (1892), 22, 467-8.



TABLE V.—*The figures from Table IV reduced to 50 kilograms body weight.*

Number of experiment.	Calories.	Nitrogen intake.	Nitrogen balance.	Diet.
		<i>Per cent.</i>	<i>Per cent.</i>	
4	2,250	5.0	−1.6	Rice, bacon, sugar, coffee, bananas, rice cake.
2	2,200	5.5	−0.8	
1	2,200	5.5	−1.7	
3	2,200	6.0	−1.6	
5	2,050	7.5	−3.5	Rice, bread, bacon, sugar, coffee, phytin (No. 6), egg albumin (No. 7).
6	2,050	7.5	−1.6	
7	2,050	8.5	−1.5	
14	1,500	8.5	−0.9	
8	1,950	9.0	−0.4	Rice, bread, fish, sugar, coffee, and bananas, rice cake (No. 8), rice polishings (No. 11).
9	1,900	9.0	+0.1	
12	1,550	9.5	−0.6	
13	1,550	9.5	−0.6	
10	1,850	10.5	+0.4	
11	1,850	11.5	+0.5	

It was not possible to establish nitrogen equilibrium, even in cases where the nitrogen intake was comparatively high, if the number of calories taken was below 1,800 for 50 kilograms of body weight (see experiments numbered 12, 13, 14); on the other hand, if the number 1,800 was equalled or exceeded, then 9 grams of nitrogen per 50 kilograms of body weight were sufficient. If a less quantity of nitrogen than the above figure was taken with the food, then the loss of nitrogen exceeded the amount taken, even if the number of calories reached 2,200. However, with an intake of 5 to 6 grams of nitrogen, the deficit amounted to less than 2 grams (see experiments numbered 1 to 4). Consequently, we are justified in concluding that in some instances 8 grams of nitrogen per 50 kilograms, or 0.16 gram per kilogram of body weight are sufficient. This value is higher than the lowest limit found by other authors, who succeeded in establishing nitrogen equilibrium on 0.1 gram per kilogram of body weight.

The question as to whether the quantity of protein given in a certain food will be sufficient or not, is mainly influenced by the proportion of protein absorbed, for that protein which is excreted, unabsorbed, by means of the faeces, obviously is worthless for the nutrition of the body. If from this point of view we consider the nitrogen absorption in our experiments, it appears that a subject, given a diet of pure rice, excretes in the faeces about 30 per cent (experiments numbered 1 and 2), and even

47 per cent (experiment number 4) of the nitrogen taken. The nitrogen contained in the outer layers of the rice, whether taken with the grain (experiment number 3), or in the form of the material milled off from the grain and added to the food (experiment number 11) is absorbed only to the extent of about 25 per cent. Therefore, the fact that the nitrogen content of red rice is somewhat higher than that of the white variety is of no physiological importance.

Rübner found about 75 per cent of the nitrogen in rice to be absorbed, Mori as much as 78.3 per cent. On the other hand, Thomas and Yukawa give values agreeing more closely with ours, namely, 67.4 per cent and 66.1 per cent, respectively.

The nitrogen in the faeces does not consist solely of that not absorbed from the foodstuffs, but it is partly present as nitrogen from the secretions of the intestinal tract. Therefore, the quantity of unabsorbed nitrogen, expressed in percentage of the nitrogen taken, must be proportionally higher the lower the nitrogen intake is. This explains the fact that not only in our work, but also in that of Thomas<sup>9</sup> and Yukawa,<sup>10</sup> a lower percentage of the nitrogen taken was found to be absorbed, even with a lower nitrogen intake, than was the case in the experiments of Rübner,<sup>11</sup> Kellner, and Mori. The percentage of absorption of nitrogen when the diet consists of bread and rice is practically the same as in the case of white rice alone. This is made plain by comparing experiments numbered 5 to 7 with numbers 1 and 2.

The experiments with mixed diet are interesting, as is shown by Table VI.

TABLE VI.—*Experiments with mixed diet.*

Experiment number.	In the food.			Quantity of nitrogen in faeces.	Absorption of nitrogen.	Nitrogen of faeces in per cent of animal nitrogen in food.
	Animal nitrogen.	Vegetable nitrogen.	Total nitrogen.			
	Grams.	Grams.	Grams.	Grams.	Per cent.	Per cent.
5	0.31	9.26	9.57	3.39	64.6	36.5
6	0.25	9.16	9.41	3.23	65.7	35.2
7	1.95	9.11	11.06	3.38	69.4	37.1
10	2.52	8.47	10.99	2.64	76.0	31.2
13	4.37	5.90	10.27	2.27	77.9	38.5
12	4.37	5.90	10.27	2.03	81.0	36.0
8	4.26	5.66	9.92	2.15	78.3	37.9
14	2.62	5.28	7.90	1.98	74.9	37.5
9	2.84	4.76	7.60	1.64	78.4	34.4

The smaller the proportion of vegetable nitrogen in the food the greater relatively, is the absorption of nitrogen. The nitrogen content of the faeces is practically directly proportional to the quantity of vegetable nitrogen in the food, and is influenced but little by the amount in the

<sup>9</sup> *Loc. cit.*

<sup>10</sup> *Arch. Verd. Kreht.* (1910) **15**, 4-5.

<sup>11</sup> *Ztschr. Biol.* (1889) **25**, 102-22.

animal constituents. For this reason, the quantity of nitrogen in the fæces, expressed in percentages of the vegetable nitrogen in the food, is practically a constant value of 35 per cent. Therefore, it is necessary to know the relative value between the protein of animal and of vegetable origin in order to determine the physiologic value of the protein content of a given food. Nearly one-third of the protein from rice and wheat passes unabsorbed through the intestines into the fæces; this must be subtracted as physiologically valueless.

According to the recent investigations by Michaud<sup>12</sup> and by Thomas,<sup>13</sup> the biologic value of various classes of proteins differs widely. Therefore, protein in rice certainly would have a lower biologic value than protein from animal sources. It is to be regretted that our knowledge of the chemical composition of the protein of rice is so meager, whereas many detailed investigations on other vegetable proteins of considerably minor importance exist.

Finally, we wish to emphasize the fact that the absorption of nitrogen can be determined only by an exact knowledge of the nitrogen content of the fæces. The quantity of the nitrogen absorbed is equal to the quantity ingested, minus the amount in the fæces. The quantity of nitrogen excreted in the urine is equal to the amount absorbed only in case the subject is in exact nitrogenous equilibrium, so that miscalculations would result in many instances if the former figures were to be taken.

#### PHOSPHORUS METABOLISM.

A summary of our experiments is given in Table VII; the quantity of phosphorus ingested and the phosphorus balance being reduced to 50 kilograms of body weight.

TABLE VII.—*Phosphorus metabolism reduced to 50 kilograms body weight.*

Experi- ment number.	P <sub>2</sub> O <sub>5</sub> intake.	P <sub>2</sub> O <sub>5</sub> balance.
	<i>Per cent.</i>	<i>Per cent.</i>
5	1.15	—0.8
4	1.45	—0.45
7	1.45	—0.3
10	1.60	+0.01
14	1.60	—0.10
9	1.65	—0.01
12	1.65	—0.2
13	1.65	—0.1
3	3.30	+0.16
6	3.85	+1.2
11	5.20	+0.6

<sup>12</sup> *Ztschr. f. phys. Chem.* (1907), **59**, 405–91.

<sup>13</sup> *Loc. cit.*

While it is not possible to establish an exact phosphorus minimum, just as it is impossible to establish a nitrogen minimum, our experiments show that an intake of less than 1.65 grams of phosphorus per 50 kilograms of body weight, or 0.033 grams phosphoric anhydride per kilogram is insufficient to cover the demand of the body for phosphorus. The quantities given by most authors<sup>14</sup> are considerably higher than this figure.

We discussed the fact that the phosphorus content of rice is of very great physiologic importance, in the introduction to this paper. Experiments numbered 4, 5, and 7 show conclusively that a diet consisting of white rice, bread, bacon, and other foodstuffs poor in phosphorus does not cover the demand of the body for that element, even with the addition of small quantities of fish. (See experiments numbered 12, 13, and 14.) However, the phosphorus balance becomes positive if unpolished rice, rice bran, or phytin is added to the food. (See experiments numbered 3, 6, and 11.) A comparison of experiments numbered 3 and 4 very plainly shows that the body loses phosphorus when on a diet consisting mainly of white rice, while on the same diet, red rice being substituted, the amount of that element exceeds the demand of the body. The distribution of phosphorus in urine and feces is not of as great importance as in the case of nitrogen, because the phosphorus excreted in the feces consists in part of that which has previously been absorbed and again excreted in the lower parts of the large intestines. It should be noted that those experiments where the amount of phosphorus taken was high show that the excess is excreted almost entirely in the feces.

Our figures seem to show that the phosphorus demand of Filipinos (Malays) is lower than that given by other authors. It may be that the body becomes accustomed to a lower supply of phosphorus than that usually considered to be necessary, and the high results in the metabolism experiments on Europeans might simply be requirements of "luxury." Another view seems not too far removed: Several authors have argued that there is a connection between mental work and phosphorus metabolism. Of course, the belief of older investigators, that mental work increases metabolism in the brain, which is rich in phosphorus, has been shown to be absurd. The quantity of phosphorus in the brain itself is much too small as a whole to influence the phosphorus metabolism of the body. However, the nervous system might have a regulatory influence on all the dissimilative processes in the body, so that what we might term the "tone" of the "catabolic cell-metabolism" could be increased during intensive activity of the nervous system and lowered during rest. We have based this consideration especially on the very striking results of experiments by Folin and Shaffer. If such a view has any basis in fact, then the "tone" of the cell metabolism of the ordinary Malay, with his phlegmatic temperament, must be very low. Such a conclusion is somewhat startling. Once considered, it was necessary to attempt to demonstrate whether a difference in the destruction of

<sup>14</sup> Oeri, *Ztschr. klin. Med.* (1909), **67**, 288, 306; Ehvstrohm, *Skand. Arch. Phys.* (1903), **14**, 91; Renoall, *Skand. Arch. Phys.* (1905), **16**, 94-138; R. Tigerstedt, *Handbuch d. Phys.* (Nagel) (1908), **1**, 530.

the body material containing phosphorus takes place in ordinary Filipinos, as shown by an increased excretion of phosphorus in the urine, during periods of mental work and control periods, in which the subjects are left entirely to themselves, the diet being the same. With three prisoners (D, E, H) we divided the entire period into three sub-periods, during which on the one hand the men were either quiet, by themselves or, on the other hand, performed mental work. It was very easy to obtain "mental rest," but much more difficult to secure "mental work." The men were asked to study arithmetic or history, or to read poems either in Tagalog, English, or Spanish, but it was almost impossible to make them do this for more than two or three hours a day, and we are sure that when we were not present there was very little work done. One experiment, number 9, apparently gave a decidedly positive result; experiment number 15 was practically indecisive; and experiments numbered 12 and 13, which seemed to be the most successful of all, apparently gave exactly the opposite result, if differences could be considered to be present at all.

Table VIII shows the influence of mental work and mental rest on the phosphorus excretion in the urine, so far as our experiments go. We do not believe that any definite conclusion can be drawn from them.

TABLE VIII.—Nitrogen and phosphoric anhydride excretion in the urine during periods of rest and mental work.

*Experiment 9, Prisoner D.*

Condition.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .
	Grams.	Grams.
Rest 2 days	11.01	1.42
Mental work 2 days	12.96	1.85
Rest 2 days	11.41	1.56

*Experiment 15, Prisoner H.*

Condition.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .
	Grams.	Grams.
Rest 2 days	13.75	2.14
Mental work 2 days	13.77	2.42

*Experiments 12-13, Prisoner E.*

Condition.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .
	Grams.	Grams.
Rest 3 days:		
First day	9.09	1.65
Second day	8.80	1.13
Third day	9.01	0.91
Mental work 3 days:		
First day	8.66	1.08
Second day	8.41	0.98
Third day	9.13	1.28
Rest 2 days:		
First day	8.45	1.29
Second day	8.76	1.25

TABLE IX.—Complete records of the experiments and analyses of foodstuffs.

Numbers of experiments.	Foodstuff.	N.	P <sub>2</sub> O <sub>5</sub> .
		Per cent.	Per cent.
9, 12, 13, 14, 15	Bread	1.28	0.17
1, 2	Rice I	1.109	
3	Rice r	1.29	0.77
4	Rice w	1.26	0.32
8	Rice II	1.116	
9	Rice A	1.29	0.28
12, 13, 14, 15	Rice B	1.23	0.37
1, 2	Rice cake I	0.405	(a)
8	Rice cake II	0.423	
1, 2	Bacon I	0.82	(b)
3, 4	Bacon II	0.75	0.056
8	Fish (dalag)	3.556	
9	Fish (salmon)	3.60	0.40
12, 13, 14, 15	Salt codfish	4.37	0.346
3, 4	Onions	0.14	0.06
		Gram.	Gram.
1, 2, 8	Coffee 150 cc	0.02	
3, 4, 9, 12, 13, 14, 15	Coffee 500 cc	0.02	0.016

a Fat 12.2 per cent.

b Fat 86 per cent.

EXPERIMENT NO. 1.—September 22 to 24, 1910 (subject, medical student V; weight, 53.7 kilograms).

Daily food.		Nitrogen.	Calories (estimated).
		Grams.	
400 grams rice I		4.44	1,300
200 grams rice cake I		0.81	340
100 grams bananas		0.22	80
45 grams sugar			160
60 grams bacon I		0.49	480
150 grams coffe		0.02	
Total intake per day		5.98	2,360

Day.	Analyses of urine.		Analyses of fæces.
	Quantity.	Nitrogen.	
	cc.	Per cent.	
September 22	530 (1,000)	6.09	61.5 grams fæces containing 8.80 per cent nitrogen and 94.9 per cent solids. Total nitrogen, 5.31 grams.
September 23	560 (1,000)	5.75	
September 24	880 (1,000)	5.76	
Total nitrogen		17.60	

*Balance sheet, per day.*

	Grams of nitrogen.
Outgo in urine	5.87
Outgo in fæces	1.77
Total outgo	7.64
Intake, total	5.98
Balance	1.66

EXPERIMENT No. 2.—September 22 to 24, 1910 (subject, medical student F; weight, 54.0 kilograms).

Daily food.		Nitrogen.	Calories (estimated).
		Grams.	
400 grams rice I		4.44	1,300
200 grams rice cake I		0.81	340
150 grams bananas		0.33	120
45 grams sugar			160
60 grams bacon I		0.49	480
150 grams coffee		0.02	
Total intake per day		6.09	2,400

Day.	Analyses of urine.		Analyses of fæces.
	Quantity.	Nitrogen.	
	cc.	Per cent.	
September 22	930	4.87	75.0 grams dried fæces containing 8.28 per cent nitrogen and 94.6 per cent solids. Total nitrogen, 6.19 grams.
September 23	1,075	4.92	
September 24	725	4.78	
Total nitrogen		14.57	

*Balance sheet, per day.*

	Grams of nitrogen.
Outgo in urine	4.86
Outgo in fæces	2.06
Total outgo	6.92
Intake, total	6.09
Balance	—0.83

EXPERIMENT NO. 3.—November 16 to 21, 1910 (subject, prisoner C; weight, 49.0 kilograms).

Daily food.				Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories (estimated).
				Grams.	Grams.	
400 grams rice r				5.16	3.08	1,350
100 grams onions				0.14	0.06	50
50 grams bacon II				0.38	0.03	350
300 grams coffee				0.15	0.05	
20 grams lard						150
50 grams sugar						200
Total intake per day				5.83	3.22	2,200

Analyses of urine.				Analyses of fæces.	
Day.	Quantity.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .		
	cc.	Per cent.	Per cent.		
November 18	640	17.05	4.129	{ 204 grams dried fæces containing 6.11 per cent nitrogen and 3.97 per cent P <sub>2</sub> O <sub>5</sub> . Total, 12.46 grams nitrogen and 8.10 grams P <sub>2</sub> O <sub>5</sub> .	
November 19	400				
November 20	400				
November 21	480				

Balance sheet, per day.

	Grams of nitrogen.	Grams of P <sub>2</sub> O <sub>5</sub> .
Excretion in urine	4.26	1.03
Outgo in fæces	3.11	2.03
Total outgo	7.37	3.06
Intake, total	5.83	3.22
Balance	−1.54	+0.16

EXPERIMENT NO. 4.—November 22 to 25, 1910 (subject, prisoner C; weight, 48.6 kilograms).

Daily food.				Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories (estimated).
				Grams.	Grams.	
400 grams rice W				4.24	1.28	1,350
100 grams onions				0.14	0.06	
50 grams bacon II				0.38	0.03	350
300 grams coffee				0.15	0.05	
20 grams lard						150
50 grams sugar						200
Total intake per day				4.91	1.42	2,200

Analyses of urine.				Analyses of fæces.	
Day.	Quantity.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .		
	cc.	Grams.	Grams.		
November 22	2,425	17.04	4.16	{ 132.4 grams dried fæces containing 7.05 per cent nitrogen and 2.50 per cent P <sub>2</sub> O <sub>5</sub> . Total, 9.33 grams nitrogen and 3.31 grams P <sub>2</sub> O <sub>5</sub> .	
November 23	1,305				
November 24	850				
November 25	980				



Balance sheet, per day.

	Grams of nitrogen.	Grams of P <sub>2</sub> O <sub>5</sub> .
Outgo in urine	4.26	1.04
Outgo in fæces	2.33	0.83
Total outgo	6.59	1.87
Intake, total	4.91	1.42
Balance	-1.68	-0.45

EXPERIMENT NO. 8.—September 27 to October 1, 1910 (subject, medical student F; weight, 54.0 kilograms).

Daily food.			Nitrogen.	Calories (estimated).
			Grams.	
400 grams rice II			4.46	1,300
120 grams fish (dalag)			4.26	100
150 grams bananas			0.33	120
200 grams rice cake II			0.85	340
40 grams sugar				160
150 grams coffee			0.02	
10 grams lard				80
Total intake per day			9.92	2,100

Day.	Analyses of urine.		Analyses of fæces.
	Quantity.	Nitrogen.	
	cc.	Grams.	
September 27	690	7.37	46 grams dried fæces containing 6.85 per cent nitrogen and 98 grams dried fæces containing 7.73 per cent nitrogen. Total, 10.73 grams nitrogen (5 days).
September 28	915	7.60	
September 29	1,475	9.09	
September 30	1,315	8.71	
October 1	Lost.		
Total		32.77	

\*4 days.

Balance sheet, per day.

	Grams of nitrogen.
Outgo in urine	8.20
Outgo in fæces	2.15
Total outgo	10.35
Intake, total	9.92
Balance	-0.43

EXPERIMENT NO. 9.—*June 27 to July 3, 1910 (subject, prisoner D; weight, 43.5 kilograms).*

Daily food.		Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories (estimated).
		Grams.	Grams.	
200 grams rice A		2.57	0.56	650
150 grams bread		1.93	0.24	300
75 grams salmon		2.84	0.32	100
150 grams sugar				600
500 grams coffee		0.26	0.16	
Total intake per day		7.60	1.28	1,650

Day.	Analyses of urine.			Analyses of fæces.
	Quantity.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	
	cc.	Grams.	Grams.	
June 27	1,110	11.01	1.419	140 grams dried fæces containing 7.02 per cent nitrogen and 2.08 per cent P <sub>2</sub> O <sub>5</sub> . Total, 9.83 grams nitrogen and 2.91 grams P <sub>2</sub> O <sub>5</sub> .
June 28	980			
June 29	890	12.96	1.848	
June 30	855			
July 1	1,145	11.41	1.563	
July 2	630			
Total		35.38	4.830	

*Balance sheet, per day.*

	Grams of nitrogen.	Grams of P <sub>2</sub> O <sub>5</sub> .
Outgo in urine	5.90	0.80
Outgo in fæces	1.64	0.49
Total outgo	7.54	1.29
Intake, total	7.60	1.28
Balance	+0.06	−0.01

EXPERIMENT NO. 12.—*July 23 to 25, 1910 (subject, prisoner E; weight, 54.0 kilograms).*

Daily food.		Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories (estimated).
		Grams.	Grams.	
250 grams rice B		3.075	0.925	800
200 grams bread		2.56	0.34	400
100 grams salt codfish		4.37	0.346	150
100 grams sugar				400
500 grams coffee		0.26	0.16	
Total intake per day		10.265	1.77	1,750

EXPERIMENT No. 12.—*July 23 to 25, 1910 (subject, prisoner E; weight, 54.0 kilograms)*—Continued.

Day.	Analyses of urine.			Analyses of fæces.
	Quantity.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	
	cc.	Grams.	Grams.	
July 23 -----	2,030	9.09	1.65	} 74 grams containing 8.26 per cent nitrogen and 3.01 per cent P <sub>2</sub> O <sub>5</sub> . Total, 6.112 grams nitrogen and 2.29 grams P <sub>2</sub> O <sub>5</sub> .
July 24 -----	1,250	8.80	1.13	
July 25 -----	830 (1,000)	9.01	0.91	
Total -----		26.90	3.69	

*Balance sheet, per day.*

	Grams of nitrogen.	Grams of P <sub>2</sub> O <sub>5</sub> .
Outgo in urine	8.96	1.23
Outgo in fæces	2.03	0.76
Total outgo	10.99	1.99
Intake, total	10.27	1.77
Balance	-0.72	-0.22

EXPERIMENT No. 13.—*July 26 to 30, 1910 (subject, prisoner E; weight, 54 kilograms).*

Daily food.		Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories (estimated).
		Grams.	Grams.	
250 grams rice B -----		8.075	0.925	800
200 grams bread -----		2.56	0.34	400
100 grams salt codfish -----		4.37	0.346	150
100 grams sugar -----				400
500 grams coffee -----		0.26	0.16	
Total intake per day -----		10.265	1.77	1,750

Day.	Analyses of urine.			Analyses of fæces.
	Quantity.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	
	cc.	Grams.	Grams.	
July 26 --	660 (1,000)	8.66	1.08	} 95 grams dried fæces containing 7.18 per cent nitrogen and 2.30 per cent P <sub>2</sub> O <sub>5</sub> . Total, 6.82 grams nitrogen and 2.19 grams P <sub>2</sub> O <sub>5</sub> .
July 27 --	640 (1,000)	8.41	0.98	
July 28 --	670 (1,000)	9.13	1.28	
July 29 --	600 (1,000)	8.45	1.29	
July 30 --	580 (1,000)	8.76	1.25	

*Balance sheet, per day.*

	Grams of nitrogen.	Grams of P <sub>2</sub> O <sub>5</sub> .
Outgo in urine	8.73	1.11
Outgo in fæces	2.27	0.76
Total outgo	11.00	1.87
Total intake	10.27	1.77
Balance	-0.73	-0.10

EXPERIMENT NO. 14.—August 10 to 14, 1910 (subject, prisoner G; weight, 45.9 kilograms).

Daily food.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories (estimated).
	Grams.	Grams.	
200 grams rice B	2.46	0.74	650
200 grams bread	2.56	0.34	400
50 grams sugar			200
60 grams salt codfish	2.62	0.21	100
500 grams coffee	0.26	0.16	
Total intake per day	7.90	1.45	1,350

Day.	Analyses of urine.			Analyses of fæces.
	Quantity.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	
	cc.	Grams.	Grams.	
August 11	830	26.88	3.796	{ 114 grams dried fæces containing 6.93 per cent nitrogen and 2.04 per cent phosphoric anhydride. Total, 2.33 grams phosphoric anhydride and 7.90 grams nitrogen.
August 12	1,020			
August 13	1,570			
August 14	1,550			

*Balance sheet, duration 4 days.*

	Grams of nitrogen.	Grams of phospho- ric anhy- dride.
Outgo urine	6.72	0.949
Outgo fæces	1.985	0.583
Total outgo	8.705	1.532
Total intake	7.90	1.45
Balance	-0.80	-0.08

EXPERIMENT No. 15.—*June 16 to 21, 1910 (subject, prisoner H; weight, 53.0 kilograms).*

Daily food.	Nitrogen.	P <sub>2</sub> O <sub>5</sub> .	Calories. (estimated).
	<i>Grams.</i>	<i>Grams.</i>	
250 grams rice B.....	3.08	0.93	800
200 grams bread.....	2.56	0.34	400
60 grams salt codfish.....	2.62	0.21	100
75 grams sugar.....			300
500 grams coffee.....	0.26	0.16	
Total intake per day.....	8.52	1.64	1,600

*Analyses of urines.*

Day.	Quantity.	Nitrogen.	Phosphoric anhydride.
	<i>cc.</i>	<i>Grams.</i>	<i>Grams.</i>
June 17.....	1,050	7.30	
June 18.....	840	13.75	2.135
June 19.....	725		
June 20.....	550	13.77	2.42
June 21.....	1,030		

*Balance sheet, duration 4 days.*

	Grams of nitrogen.	Grams of phospho- ric anhy- dride.
Outgo urine	6.87	1.21
Outgo fæces	.....	.....
Total outgo	.....	.....
Total intake	8.52	1.63
Balance	.....	.....



# THE EFFECT OF ULTRA-VIOLET RAYS ON AMOEBAE, AND THE USE OF THESE RADIATIONS IN THE STERILIZATION OF WATER.<sup>1</sup>

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By WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.<sup>2</sup>

(From the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.<sup>3</sup>)

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It has already been shown by several investigators that the ultra-violet rays of the spectrum are capable of killing bacteria in a few seconds, and the Westinghouse Cooper Hewitt Company of London and Paris have constructed several types of practical water sterilizers utilizing these rays. The ultra-violet radiation, upon which the action of these sterilizers depends, is produced by a quartz mercury-vapor lamp either suspended over or immersed in the water. One type has a capacity of 132,000 gallons (528,000 liters) of potable water in twenty-four hours, and only requires an electric current of three or three and one-half amperes at 220 volts for its operation. It has been demonstrated by experimentally polluting water with *Bacillus coli* that these organisms are killed during the passage through such a sterilizer, although the water remains in the apparatus for only five seconds. A more complete description, together with photographs and diagrams of this apparatus, may be obtained from the articles of Foulds<sup>(1)</sup> and Thresh and Beale.<sup>(2)</sup>

There are many features about this method of sterilization that render it peculiarly suitable for use in tropical countries and by armies in the field, among which the following may be mentioned. It is automatic and can be intrusted to a comparatively unskilled man, this automatic action being secured by a valve in the inlet which is operated by the current of the same circuit that produces the rays, and which prevents

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<sup>2</sup> W. P. Chamberlain, major, Medical Corps, United States Army, and E. B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

<sup>3</sup> The apparatus for these experiments was supplied by the Bureau of Science, and the exposures were made in that Bureau.

any water from entering the sterilizer if the current is interrupted. The apparatus is small and one type is portable. The water is neither heated nor altered in taste by the process. It provides a rapid method by which a badly polluted water may be transformed into one of potable quality, and finally it is very economical in operation. The low cost should place it within the means even of poor native villages, a small gasoline engine being capable of producing sufficient power.

For army use this apparatus with dynamo and gasoline engine could be readily carried in an escort wagon or automobile. In case the latter were used a special gasoline engine could be dispensed with, and the motor of the automobile utilized to drive the dynamo. The small type of apparatus delivers 130 gallons (520 liters) of sterile water per hour, and it would be capable of supplying an entire regiment with a quart of water for each man after only three hours' operation. The larger apparatus, although designed for permanent installation, could also be carried in an escort wagon, and would supply 132,000 gallons (528,000 liters) in twenty-four hours, thus providing in twelve hours a little over 3 gallons (12 liters) of sterile water for every soldier in a division of 20,000 men. The delivery of pure water would commence within a few minutes after arrival in camp, would be continuous, and the water would be unchanged in taste, a great desideratum when dealing with soldiers whose objection to the flat taste of boiled water is well known. Also there would be no time wasted in waiting for water to cool as is the case when sterilization by heat is resorted to.

But in considering the use of such a sterilizer in the Tropics we are confronted by the fact that bacterial pollution is not the only nor, in some cases, the most important danger that lurks in the drinking supply. Amœbæ are found in practically all tropical surface waters, and while the free-living species are not pathogenic, it is to be expected that *Entamœba histolytica* will be encountered under the same conditions of pollution that would cause the presence of typhoid bacilli or cholera spirilla in the water. In similar circumstances, *Balantidium coli*, *Lamblia intestinalis*, and other protozoa, as well as the ova or larvæ of various parasites are liable to occur. Therefore it is important, before adopting any method of water purification for tropical countries, to show that the procedure will protect the consumers against infections with animal parasites as well as against the bacterial causes of disease. Filter beds will eliminate 99 per cent of the bacteria in water, but will not remove amœbæ or other protozoa, so that this method of water purification is impracticable in the Philippines for this reason and also because of its great expense.

It seems quite probable, from what we know of the action of the



ultra-violet radiation, that protozoa and the ova or larvæ of intestinal worms may all be killed by this powerful agent. It has been shown<sup>(3)</sup> that radium emanations on short exposures inhibit, and on longer exposures kill various forms of bacteria, protozoa, ova, embryos, and larvæ. The only reference we have found indicating that the effects of ultra-violet rays have been tested with protozoa is an article by Hertel<sup>(4)</sup> showing that paramœcia are killed by these short length waves. We have failed to find in Manila any reference indicating that the influence of ultra-violet rays on amœbæ has been investigated.

These considerations seemed to indicate the desirability of studying the effect of ultra-violet rays on amœbæ and the experiments about to be described were undertaken for this purpose. The source of the ultra-violet radiations used by us was a quartz mercury-vapor arc lamp owned by the Bureau of Science in Manila. This lamp, which was made by the firm of W. C. Heraeus, Hanau, Germany, was rather small for our purpose, but produced a brilliant light particularly rich in ultra-violet rays. A description of the lamp may be found in the *Zeitschrift für Electro-chemie*.<sup>(5)</sup>

The strain of amœbæ used was originally isolated from a normal human stool, has been kept constantly under cultivation for a year, and is the same that was employed previously to determine the efficacy of the ipecac treatment of dysentery.<sup>(6)</sup> These amœbæ belong undoubtedly to a free-living species, but it is believed that any agent which is found to be detrimental to the growth of such free-living organisms will prove even more efficacious against the parasitic amœbæ which are much more susceptible to unfavorable conditions as shown by the fact that it has hitherto been impossible to cultivate them on artificial media.

The experiments were performed in a number of ways, using both solid and fluid media, and with exposures for different periods of time at various distances from the source of radiation. After the exposure, cultures were made at once from the exposed amœbæ to determine whether they had been killed by the rays, and these observations were controlled by similar cultures made from amœbæ grown under identical circumstances, but which had not been subjected to the action of ultra-violet waves. The effect of the rays on the amœbæ has also been compared with the effect produced on *Bacillus typhosus* and *Bacillus dysenteriae* (Shiga) by similar exposures. Before proceeding to an account of the experiments themselves we will give a brief description of the stock culture of amœbæ and the plates used, and the method of exposing the cultures to the rays.

A. *Stock culture of amœbæ*.—The amœbæ referred to previously were cultivated for several weeks in a 250 cubic centimeter Erlenmeyer flask containing plain

bouillon mixed with double the quantity of distilled water. During this period the flask was handled with care so that the fluid was never shaken, and the amœbæ that developed were found in countless numbers lying in the surface film of the bouillon. This flask was then used as a stock culture from which all the inoculations of an experiment were made, and a single large loopful taken from this surface film was used for each inoculation.

B. *Plates*.—The lamp already referred to is in the form of a small arc and the rays, both visible and invisible, radiate from this arc in every direction. The radiations diminish in intensity as the square of the distance from the source, and therefore it was desirable to make the exposures quite close to the lamp, approximately 10 centimeters from it. But it seemed probable, if ordinary-sized Petri dishes were used at this distance, that the outer margins of the plate might be beyond the sphere of effective intensity of the rays, and that for this reason some of the amœbæ might not be killed. In order to avoid this difficulty we used special plates consisting of aluminum ointment boxes 2.5 centimeters in diameter and with tightly fitting covers. These boxes were sterilized in the autoclave, filled with plain sterile agar and covered with their lids. This kind of plate avoided the difficulty just mentioned, and was very convenient to handle, took up less space in the incubator, and required much less agar, points by no means beneath consideration when it is a question of making several hundred exposures.

C. *Method of making exposures*.—The inoculated plate was uncovered and placed directly under the center of the lamp. The cover was turned upside down and placed beside the plate in order that it should also be exposed to the rays with a view to killing any amœbæ that might have contaminated it accidentally. The switch controlling the current operating the lamp was then closed and the appearance of the light timed with a watch. After the desired number of seconds of exposure, the switch was opened. We were thus enabled to time our exposures accurately. As soon the exposure was completed the cover was replaced on the plate.

This method was quite satisfactory except for one particular. We know that it is necessary for the lamp to become warmed up before it is capable of producing its maximum output of ultra-violet rays. This occurs a few seconds after the current is turned on, in which time the lamp becomes quite hot. It is probable that this temporary lack of efficiency in the apparatus when the current is first turned on explains why some of our cultures were not killed by exposure for a period of five seconds. This will be referred to again later.

In order to prove that the amœbæ and bacteria were killed by the ultra-violet rays, and not by heat generated by the lamp, we exposed a thermometer 10 centimeters from the lamp, that being the nearest point at which the cultures were ever placed. After a forty-second exposure the thermometer had risen to 50° centigrade. Thus it is shown that although the lamp itself may become very hot, sufficient heat to injure bacteria or amœbæ is not radiated to a distance of 10 centimeters in a period of forty seconds. Only a slight sensation of warmth is felt if the hand is exposed close to the lamp, although a severe burn might be caused if the lamp itself were actually touched.

*Experiment I*.—In this experiment plates made as described above were exposed to the ultra-violet rays immediately after they were ino-

culated. Part of these plates were inoculated with a loopful from the stock culture of amœbæ, part from a stock culture of *Bacillus typhosus*, and part from a stock culture of *Bacillus dysenteriae*. A few of the plates inoculated with each organism were at once placed in the incubator to serve as controls while the remainder were exposed to the rays as described above, for periods varying from five to eighty seconds, and after the exposure they also were placed in the incubator. In order to compare the effects of the rays at different distances from their source, exposures were made at point 10, 15, and 23 centimeters from the lamp. After incubation for twenty-four hours, the plates were examined for growth and the results of this experiment are contained in Table I. In this as in subsequent tables, the plus sign means that growth occurred, while the minus sign indicates a sterile plate or culture.

TABLE I.—*Experiment 1: Agar plates exposed to ultra-violet rays immediately after inoculation, and then incubated 24 hours.*

Distance from lamp.	No.	Organism exposed.	Time of exposure in seconds.								Con- trols, not ex- posed.	
			5	10	20	30	40	50	60	70		80
A. 10 cm.	1	Amœbæ -----	—	—	—	—	—	—	—	—	—	+
	2	Amœbæ -----	—	—	—	—	—	—	—	—	—	+
	3	B. typhosus -----	—	—	—	—	—	—	—	—	—	+
	4	B. typhosus -----	+(6)	—	—	—	—	—	—	—	—	+
	5	B. dysenteriae -----	+(2)	—	—	—	—	—	—	—	—	+
	6	B. dysenteriae -----	—	—	—	—	—	—	—	—	—	+
B. 15 cm.	7	Amœbæ -----	—	—	—	—	—	—	—	—	—	+
	8	Amœbæ -----	—	—	—	—	—	—	—	—	—	+
	9	B. typhosus -----	—	—	—	—	—	—	—	—	—	+
	10	B. typhosus -----	—	—	—	—	—	—	—	—	—	+
	11	B. Dysenteriae -----	+(1)	—	—	—	—	—	—	—	—	+
	12	B. Dysenteriae -----	+(2)	—	—	—	—	—	—	—	—	+
C. 23 cm.	13	Amœbæ -----	+	+	+	+	+	+	+	—	—	+
	14	Amœbæ -----	+	+	+	+	+	+	+	—	—	+
	15	B. typhosus -----	+(3)	+	+	—	—	—	—	—	—	+
	16	B. typhosus -----	+(2)	+	+	—	—	—	—	—	—	+
	17	B. dysenteriae -----	+(4)	+	+	—	—	—	—	—	—	+
	18	B. dysenteriae -----	+(1)	+	+	—	—	—	—	—	—	+

The figures in parentheses in the 5-second column indicate the number of colonies found on the plate after incubation.

As is shown clearly in Table I, a profuse growth was found on all of the controls which were not exposed to the rays. Of the plates exposed for five seconds at 10 and 15 centimeters, some of those inoculated with bacteria showed growth and others were sterile, but none

of the plates inoculated with amœbæ showed growth after this exposure. However, it will be seen that the effect of the rays on the bacteria was very pronounced even in five-second exposures, because instead of a profuse growth such as was observed on the control plates, only a few scattered colonies were found. If the lamp had been in preliminary operation for a few seconds, so that it was producing its maximum of rays at the time the exposure began, it is probable that all of the plates exposed for five seconds would have been sterile. It would have been very difficult however to make accurately timed exposures with the lamp continuously in operation, and in any case the results are sufficient for our present purpose. Others have already demonstrated that bacteria are killed in five seconds by such exposures. This experiment shows that in exposures close to the lamp amœbæ are destroyed by the ultra-violet radiations quite as readily as *Bacillus typhosus* or *Bacillus dysenteriae*.

At a distance of 23 centimeters from the lamp it required twice as long an exposure to kill amœbæ as compared with *Bacillus typhosus* and *Bacillus dysenteriae*. This is unimportant with regard to practical sterilization of water in the apparatus as manufactured, for the reason that in these sterilizers all the water is forced to flow close to the lamp, and furthermore the lamp used is probably much more powerful than the arc employed by us.

The conclusions which can clearly be drawn from this experiment are that amœbæ are destroyed by exposure for a few seconds to ultra-violet rays, and that at 10 centimeters distances they are as readily killed by this agent as are dysentery and typhoid bacilli.

However, it was desirable to determine whether encysted amœbæ would be killed by this method, since it is quite probable that amœbæ in a water supply would usually be present in the encysted form. The following experiment was performed for this purpose.

*Experiment 2.*—Plates were inoculated exactly as in the first experiment, but were incubated for twenty-four hours before exposure. During this period of growth many of the amœbæ became encysted. Since it is impossible to tell by microscopic examination whether an encysted amœba is dead or alive, this point was determined by cultures. After exposure to the ultra-violet rays the growth was scraped from the surface of the plate and inoculated into a tube containing a mixture of 1 part of plain bouillon and 2 parts water. This culture was incubated for twenty-four hours and then examined for motile amœbæ. Cultures were also made from control plates that had not been exposed to the light. The results of this experiment are shown in Table II.

TABLE II.—*Experiment 2: Agar plates inoculated with amœbæ and cultivated for 24 hours before exposure to ultra-violet rays. Plates contained encysted forms.*

Distance from lamp.	No.	Time of exposure in seconds.					Control, not exposed.
		10	20	30	40	50	
A. 10 cm.	1	—	—	—	—	—	+
	2	+	—	—	—	—	+
	3	—	—	+	—	—	+
	4	—	—	—	—	—	+
B. 15 cm.	5	—	—	—	—	—	+
	6	—	—	—	—	—	+
	7	+	—	+	—	—	+
	8	—	+	—	—	—	+
C. 23 cm.	9	+	+	+	+	+	+
	10	+	+	+	+	+	+
	11	+	+	+	+	+	+
	12	+	+	+	+	+	+

By consulting this table it becomes apparent that exposures at a distance of 23 centimeters from the lamp were entirely ineffective, but that the amœbæ exposed at distances of 10 and 15 centimeters were invariably killed in forty seconds, and usually killed in ten seconds, although an occasional positive result was obtained even after exposures of thirty seconds. However, these failures may readily be explained. The growth of amœbæ and associated bacteria on plates at the end of twenty-four hours is dense, forming a very perceptible layer on the surface of the agar. It is well known that the ultra-violet rays of light have no greater power of penetration. Therefore some of the amœbæ in a few of the exposures have survived owing to the absorption of the rays by the superficial layers of the growth. This could not occur in water passing through a sterilizer operated by ultra-violet rays.

Since all of these plates contained many encysted amœbæ, and since positive cultures could never be obtained from those plates exposed forty seconds or more at 10 and 15 centimeters, and rarely after ten-second exposures, we are justified in concluding from this experiment that encysted amœbæ are killed on solid media by ultra-violet radiation. The subject of encysted amœbæ will be further discussed in Experiment 7, where a fluid medium was used.

The effect of ultra-violet rays upon amœbæ in a fluid medium was now tested. These experiments are considered to be of much more value than the preceding ones, because they approximated the conditions which

would obtain in the practical sterilization of water by the apparatus above described. The results are shown in the following 5 experiments.

*Experiment 3.*—A number of ordinary hollow-ground slides were sterilized and a large drop from the stock culture of amœbæ was placed in the hollow chamber of the slide. A culture was then made from this drop by transferring a small loopful from the slide to a test tube containing weak sterile bouillon. As soon as the culture was made, the slide was placed under the center of the lamp and the current turned on for a few seconds. After the exposure to the ultra-violet rays a second culture was made in a similar manner from the drop on the slide. Table III shows the results of such an experiment.

TABLE III.—*Experiment 3: Result of cultures from bouillon inoculated with amœbæ. Cultures made before and after exposure to ultra-violet rays.*

No.	10 cm. from lamp.			15 cm. from lamp.		
	Culture before exposure.	Exposure in seconds.	Culture after exposure.	Culture before exposure.	Exposure in seconds.	Culture after exposure.
1	+	5	—	+	5	+
2	+	5	—	+	5	—
3	+	5	—	+	5	+
4	+	10	—	+	10	—
5	+	10	—	+	10	—
6	+	10	—	+	10	—
7	+	20	—	+	20	—
8	+	20	—	+	20	—
9	+	20	—	+	20	—
10	+	30	—	+	30	—
11	+	30	—	+	30	—
12	+	30	—	+	30	—

It will be seen that in this experiment the amœbæ were killed in every trial at 10 centimeters from the lamp and were also killed in all exposures of ten seconds or more at a distance of 15 centimeters. This experiment was particularly satisfactory although it must be admitted that all circumstances were very favorable, since the amœbæ were in a thin layer of clear fluid.

*Experiment 4.*—This was performed in a manner similar to experiment 3. Distilled water was placed in ordinary staining dishes in sufficient quantity to form a layer 2.5 centimeters deep. This water was heavily inoculated with amœbæ from the stock culture. A loopful of this water was cultivated in a test tube of dilute bouillon in order

to prove the presence of amœbæ, the dish of water was then exposed to the ultra-violet rays, and a second culture at once made to show the effect of the exposure. The results of this experiment are shown in Table IV.

TABLE IV.—*Experiment 4: Result of cultures from water inoculated with amœbæ. Cultures made before and after exposure to ultra-violet rays; distance from lamp, 10 centimeters.*

No.	Culture before exposure.	Exposure in seconds.	Culture after exposure.
1	+	5	—
2	+	5	—
3	+	5	—
4	+	5	+
5	+	10	—
6	+	10	—
7	+	10	—
8	+	10	—
9	+	20	—
10	+	20	—
11	+	20	—
12	+	20	—
13	+	30	—
14	+	30	—
15	+	30	—
16	+	30	—

This experiment was equally satisfactory in demonstrating that motile amœbæ can readily be killed by exposure to ultra-violet rays. In order to clinch the matter two more experiments were performed.

*Experiment 5.*—Distilled water was inoculated with amœbæ, and exposed in the same manner as in the previous experiment, but instead of merely taking a loopful for cultivation after the exposure, the entire amount of water exposed was poured into a small flask containing bouillon, and this flask was examined for amœbæ after several days' cultivation.

*Experiment 6.*—This was the same as the previous experiment except that instead of distilled water, muddy water taken from the Pasig River was used. This was done in order to determine whether amœbæ would be killed in cloudy water or whether the rays would be intercepted by the particles in suspension, thus permitting some amœbæ to escape. For controls in both of these experiments a dish of the water used was inoculated and without exposure was at once poured into a flask of bouillon. These two experiments are shown in Table V.

TABLE V.—*Experiments 5 and 6: Results when clear and muddy waters were inoculated with amœbæ, exposed to ultra-violet rays and the entire amount of water poured into flasks containing bouillon; distance from lamp, 10 centimeters.*

No.	Experiment 5, clear water.		Experiment 6, muddy water.	
	Exposure in seconds.	Culture in flask.	Exposure in seconds.	Culture in flask.
1	10	—	20	—
2	10	—	20	—
3	20	—	20	—
4	20	—	30	—
5	30	—	30	—
6	30	—	30	—
7	{Control not ex- posed. }	+	{Control not ex- posed. }	+

From Table V it is evident that amœbæ were killed by the ultra-violet rays in both clear and muddy water after ten-seconds' exposure in the former case and after twenty-seconds' in the latter. Another very interesting and important point was noticed in experiment 6. The control flask that received the Pasig River water inoculated with amœbæ not only developed many amœbæ after a few days' cultivation, but also a large number of balantidia of unknown species. No balantidia were found in any of the flasks containing water which had been exposed to the ultra-violet rays. This affords very good evidence that balantidia as well as amœbæ are killed by ultra-violet rays. These balantidia are more or less constantly present in the Manila water supply and are probably harmless, but *Balantidium coli* is recognized as a dangerous parasite.

It will be remembered that in experiment 2 the encysted amœbæ on solid medium were not destroyed invariably by exposures of less than forty seconds. In order to demonstrate conclusively that encysted amœbæ may be killed by short exposures to ultra-violet radiations the following experiment was undertaken with a fluid medium, thus avoiding the possibility that some organisms were protected from the rays by the thick overlying film of amœbæ and bacteria.

*Experiment 7.*—Amœbæ from the stock culture were grown on an agar plate for forty-eight hours, at the end of which time microscopical examination showed very many encysted forms. These forms were as numerous as the active organisms. A little distilled water was poured upon



the plate and the amœbæ scraped from the agar; thus forming a suspension containing immense numbers of amœbæ, both encysted and motile. A little distilled water was then placed in a shallow dish, inoculated with one large loopful of the suspension of amœbæ, exposed to the rays and immediately thereafter poured into a flask containing weak sterile bouillon. After all inoculations and exposures had been completed the suspension of amœbæ was again examined microscopically and the presence of large numbers of encysted amœbæ demonstrated, thus proving that the encysted forms had not changed into motile forms during the course of the experiment.

The flasks into which the exposed amœbæ had been poured were incubated for forty-eight hours and then examined for the presence of the organisms. The results are shown in Table VI.

TABLE VI.—*Experiment 7: Clear water inoculated with encysted amœbæ, exposed to ultra-violet rays, and the entire amount of water poured into flasks of bouillon; distance from lamp 10 centimeters.*

No.	Time of exposure in seconds.				Controls not exposed.
	5	10	20	30	
1	—	—	—	—	+
2	—	—	—	—	+
3	—	—	—	—	—
4	—	—	—	—	—
5	—	—	—	—	—

This experiment conclusively proves that encysted amœbæ are killed by exposure to the ultra-violet rays for a period as short as five seconds.

#### CONCLUSIONS.

These experiments taken as a whole undoubtedly demonstrate that in a water supply the amœbæ, whether motile or encysted, may be killed by a comparatively short exposure to ultra-violet rays. Balantidia, also, appear to be destroyed by the same agency. These facts afford a very potent argument in favor of the use of these radiations in the practical sterilization of water in the Tropics. We have had no opportunity to test the apparatus manufactured for this purpose, but since the results of these preliminary experiments have proved so satisfactory we hope to perform this important work in the near future with a view to determining whether the rays are fatal to amœbæ and other protozoal parasites under the conditions obtaining with the commercial sterilizer in practical use.

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## A SECOND CONTRIBUTION TO THE ETIOLOGY OF BERIBERI.<sup>1</sup>

By WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.<sup>2</sup>

(*From United States Army Board for Study of Tropical Diseases.*)

Our previous paper on this subject<sup>(1)</sup> entitled A Contribution to the Etiology of Beriberi, as well as the present communication, deal exclusively with polyneuritis of fowls. Therefore it is fitting to state, as an explanation of our title, that we believe that polyneuritis gallinarum and beriberi are essentially the same disease. The identity of two diseases may be considered from several standpoints, including their etiology, pathology, and the symptom complex presented. The causes of beriberi and polyneuritis gallinarum are apparently identical, both diseases being produced by a deficiency of the same as yet unknown substance in the food, and the pathology and symptom complex of the two conditions are practically the same with the exception of the fact that œdema is commonly observed in beriberi and only rarely found in the multiple neuritis of fowls. The similarity is so striking that it is hard to avoid the conclusion that the two conditions are due to the same pathological process causing slightly different manifestations in diverse species. We should expect that two species, varying as widely as man and the domestic fowl in their anatomy and physiology, would react very differently when subjected to the same unfavorable diet of polished rice. The surprising thing, therefore, is not that there are differences in the symptomatology of beriberi and polyneuritis gallinarum, but that the similarity is as great as it is.

In a paper by Chamberlain, Bloombergh and Kilbourne<sup>(2)</sup> it was shown that in some cases polyneuritis gallinarum could be produced in fowls by prolonged starvation. This observation, however, does not conflict with the statement that the etiology of beriberi and polyneuritis

<sup>1</sup> Published with permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> W. P. Chamberlain, major, Medical Corps, United States Army and Edward B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

*gallinarum* are apparently the same. If a fowl is starved completely it is certainly deprived of the neuritis-preventing substance present in food. In such an experiment, therefore, it simply depends upon individual idiosyncrasy whether the fowl will die of starvation before neuritis can develop or vice versa. In other words it is a question whether the bird will die of general starvation or develop neuritis as a result of the absence of certain food elements necessary to nerve nutrition, a phenomenon which we will term partial starvation. In the great majority of cases the fowl will die without nerve degeneration as we should expect, but there will be a few exceptions to this rule for the following reason. Cocks fed on a diet of polished rice contract neuritis in an average of thirty days. In some instances a much longer time is required, while on the other hand many birds develop neuritis in less than thirty days. Several fowls in our experiments have contracted neuritis in nineteen days. Cocks that have been given nothing but water have lived from fourteen to twenty-three days. Therefore, it is apparent that in a few cases it may be possible for the nerve degeneration resulting from partial starvation to occur before the fowl succumbs to general starvation.

So far as we know, nothing at all resembling beriberi has ever developed in a professional faster or among men who have undergone starvation. But it has been shown by Frazer and Stanton<sup>(3)</sup> that it is necessary for men to subsist at least eighty-seven days on a diet of polished rice before cases of beriberi begin to appear, and it is extremely improbable that any man could live eighty-seven days without food. In the case of the fowl, therefore, the incubation period of polyneuritis is such that in a few instances it may fall within the time the bird can resist starvation, a condition that is impossible in the case of man. The observation that certain fowls when starved will develop neuritis is, therefore, no argument against the similarity of beriberi and polyneuritis *gallinarum*, since there is a perfectly satisfactory explanation for the presence of this phenomenon in fowls and its absence in man.

In our previous communication referred to above we showed that the neuritis of fowls could be prevented by means of an extract of rice polishings containing the following:

	Per cent.
Total solids	1.34
Ash	0.03
Phosphorous pentoxide	0.00165
Nitrogen	0.0406
Sucrose	0.88

We further showed that the neuritis-preventing substance must be soluble in cold alcohol and in cold water, and must be dialyzable. However, we stated that these results were based on a comparatively small

series of experiments and that further work would be performed to confirm the observations.

We are now able to state that these results have been fully confirmed. We have prepared this extract on a large number of occasions, and from five different lots of rice polishings. The quantitative analyses of these several extracts have varied slightly from that given above, as might be expected, but there has been no essential difference.

At different times we have fed seven groups, each of which consisted of four fowls, on polished rice combined with this extract in its pure form or after it had been modified by dialysis or by fermentation, with the following results:

*Group 1.*—Four fowls remained well at the end of seventy days.

*Group 2.*—Four fowls remained well at the end of seventy days.

*Group 3.*—Four fowls remained well at the end of one hundred days.

*Group 4.*—Three fowls remained well at the end of fifty days and one died, apparently of starvation, without evidence of neuritis.

*Group 5.*—Four fowls remained well at the end of sixty days.

*Group 6.*—Four fowls remained well at the end of fifty-four days.

*Group 7.*—Four fowls remained well at the end of thirty-nine days.

This makes a total of twenty-seven fowls that we have maintained in health on a diet of polished rice by the addition of this extract. This same rice repeatedly caused the development of neuritis within thirty days in fowls of our other experiments. Fraser and Stanton report a number of experiments in which the fowls were kept for only thirty-five days, a period within which neuritis ordinarily declares itself, but we have kept our birds from fifty to one hundred days. We have now been studying polyneuritis gallinarum for more than eighteen months and after observing a large number of fowls we think it is quite certain that no group of twenty-seven fowls could be maintained on a diet of polished rice for thirty days without the development of a single case of neuritis, unless they received some neuritis-preventing substance in addition to the rice. When this period is prolonged to fifty, seventy, and one hundred days, the results become conclusive.

Therefore, we regard it as proved that our extract of rice polishings prepared as described in our previous paper contains a neuritis-preventing principle.

By the same reasoning we regard it as proved that this neuritis-preventing substance is dialyzable. The four fowls that were kept one hundred days were fed on polished rice combined with the diffusate obtained from this extract.

In this connection it is interesting to note that after our first paper had gone to press we received the last communication published by Frazer and Stanton<sup>(3)</sup> in which they showed that the dialysate was incapable of protecting fowls from neuritis, thus independently confirming

our observation. They also stated their inability to obtain the diffusate resulting from the process of dialysis owing to its putrefaction. Therefore, it will be interesting to give in detail the method by which we succeeded.

The condensed extract was placed in a parchment bag and suspended in a glass jar containing distilled water in such a manner that the surfaces of the two liquids were on the same level. A few cubic centimeters of chloroform were then added to the bag and also to the water outside the bag, and the whole apparatus was placed in the ice box. The combined action of the cold and the chloroform prevented all decomposition and the dialysate and diffusate were perfectly sweet after ten days of dialysis. The diffusate was removed every two days, and replaced by fresh distilled water, in order that the dialyzable substances might be completely removed from the extract in the bag. These separate portions of the diffusate were subsequently mixed before feeding it to fowls. This method was effectual and enabled us to collect and test the diffusate, proving that it contains the neuritis-preventing principle.

The next step was to consider the action of the sucrose contained in this extract. It was utterly inconceivable on physiologic grounds that sucrose could have the slightest power to prevent neuritis, but since 0.88 out of 1.34 per cent of the total solids consisted of this dialyzable substance, we decided to give it a fair trial by experiment. Two separate experiments were undertaken for this purpose as follows:

*Experiment 5.*<sup>3</sup>—A quantity of extract was prepared from rice polishings as described previously, and was then inoculated with kitchen yeast and allowed to undergo fermentation in the incubator. Fermentation was very rapid for several days but finally ceased entirely. The extract was then filtered until it was absolutely clear and the microscope showed no yeast cells in the filtrate, in order to avoid adding yeast cells or their subsequent decomposition products to the extract. The alcohol formed by fermentation was then expelled by boiling the filtrate. This was subsequently diluted to its original bulk, reinoculated with yeast, and fermented again in order to make sure that the accumulation of alcohol had not stopped fermentation before all the sugar was exhausted. After assuring ourselves that the sugar was all removed from the extract by fermentation, the yeast cells were again carefully filtered out.

This extract contained all the substances extracted from rice polishings by this method with the exception of the sucrose,<sup>4</sup> and it was made in such proportion that 10 cubic centimeters of the extract would contain the substances extracted from 10 grams of polishings. A solution was

<sup>3</sup> Experiments one, two, three and four are detailed in our former article the title of which is given in reference one.

<sup>4</sup> The sucrose was undoubtedly removed. It is possible that some other substances also may have been broken up by the action of the yeasts or associated bacteria. We have some reason to think that the neuritis-preventing substance may be decomposed by action of bacteria.

also made containing 2 per cent of chemically pure sucrose in distilled water.

Eight fowls were now fed on polished rice. The first four were given a daily dose of 10 cubic centimeters of the fermented extract, while the second four were given 10 cubic centimeters daily of the solution of sucrose. The result of this experiment was as follows:

*Group A:* Four fowls fed on polished rice plus 10 cubic centimeters of fermented extract daily.—One fowl died of inanition, after thirty days having refused to eat for several weeks. This fowl did not have neuritis. The three remaining fowls were alive and well at the end of fifty days when the experiment was discontinued.

*Group B:* Four fowls fed on polished rice plus 10 cubic centimeters of a 2 per cent solution of sucrose.—One died of inanition in twenty-four days without neuritis; one developed neuritis in twenty-six days; one developed neuritis in twenty-eight days; one was alive and well at the end of fifty days when the experiment was discontinued.

Neuritis developed in 2 of the 4 fowls which received sucrose in twenty-six and twenty-eight days respectively, and did not develop during fifty days in any of 4 fowls that received the extract deprived of sucrose. This indicates that the sucrose is of no importance in the prevention of neuritis.

*Experiment 6.*—This experiment arrived at the same result as regards the inefficiency of sucrose, but in a different manner. An extract of rice polishings was prepared by the method detailed in our previous paper<sup>(1)</sup>, and was slowly filtered through bone black (animal charcoal). As is well known this kind of charcoal adsorbs many substances, but allows practically the entire bulk of the sugar in a solution to pass through. The extract as poured on the bone black was yellow in color, but the filtrate through the bone black was perfectly clear and appeared like water. However, fermentation tests, showed that this filtrate contained practically all of the sucrose present in the original extract.

The bone black remaining on the filter was then transferred to a flask and repeatedly shaken and washed with distilled water in order to remove, if possible, the ingredients separated from the extract by this substance. The attempt was only partially successful, since a clear fluid having a very faint bluish tint was obtained, as compared with the straw-colored fluid originally poured upon the bone black.<sup>5</sup>

Eight fowls were then fed on polished rice. The first 4 were given a daily dose of 10 cubic centimeters of the filtrate through bone black while the second 4 received a daily dose of 10 cubic centimeters of the substances subsequently removed from the bone black by distilled water. The result of this experiment is as follows:

<sup>5</sup> The bluish tinge is believed to have been due to some impurity in the charcoal.

*Group A:* Four fowls fed on polished rice plus 10 cubic centimeters daily of the filtrate through bone black.—Two fowls developed neuritis in twenty-two days; one fowl developed neuritis in twenty-four days; one fowl developed neuritis in twenty-six days.

*Group B:* Four fowls fed on polished rice plus 10 cubic centimeters of the washings of bone black daily.—One fowl developed neuritis in forty-one days; one fowl developed neuritis in forty-nine days; two fowls were alive and well on the fifty-sixth day when the experiment was discontinued.

In this experiment all 4 fowls that received the filtrate containing sucrose developed neuritis. This experiment and experiment 5 show conclusively that sucrose is incapable of preventing polyneuritis gallinarum.

We also have demonstrated in the last experiment that the neuritis-preventing principle is retained in a filter of bone black, and, therefore, bone black must have a strong power of adsorption for this substance. Washing the charcoal with water appears to remove *some* of the neuritis-preventing substance as shown by the fact that 2 out of 4 fowls were completely protected for at least fifty-six days, while in the case of the 2 birds which developed neuritis the disease manifested itself only after an unusually prolonged incubation period. It is probable that the neuritis-preventing principle can be extracted completely from this bone black by using other solvents and that this will afford another new method for the separation and identification of this important substance.

In addition to the experiments with extract of rice polishings just described, we have tested the neuritis-preventing properties of several other articles.

*Experiment 7.*—It has been suggested several times that beriberi and scurvy are closely allied diseases. This seems quite improbable owing to the vast difference in the pathology and symptomatology of the two conditions. Lime juice is well known to be both a preventive and a cure for scurvy, and if there is anything in the supposition that the two diseases are allied we might reasonably expect that the administration of lime juice would prevent the development of polyneuritis gallinarum. To test this hypothesis 4 fowls were fed on polished rice and were given a daily dose of 0.8 of a cubic centimeter of lime juice diluted with water to 10 cubic centimeters. This quantity for a fowl is equivalent to about 40 cubic centimeters for a man, which is ample to prevent the development of scurvy. The result of this experiment is as follows:

*Group A:* Four fowls fed on polished rice plus 0.8 cubic centimeter of lime juice daily.—One fowl died of inanition on the twenty-fourth day; one fowl developed neuritis on the twenty-fifth day; one fowl developed neuritis on the thirty-sixth day; one fowl was alive without neuritis, although rather weak on the thirty-ninth day when the experiment was discontinued.



Two fowls out of 4 developed neuritis while receiving lime juice daily. Therefore, it is apparent, that there is nothing in lime juice which will prevent polyneuritis gallinarum and it seems quite probable that there can be no etiological similarity between scurvy and either polyneuritis gallinarum or beriberi.

It has been suggested by several authors that neuritis of fowls and beriberi are due to a lack of nucleins in the food. The nucleins are combinations of an albumin with nucleic acid, a very complex substance containing a considerable proportion of phosphorus. Our experiments have excluded such a substance from consideration since it would not be dialyzable, and since it has been shown in our former article<sup>(1)</sup> that phosphorus is immaterial and unnecessary in preventing neuritis. We desired, however, to experiment with nuclein in order that we might have a direct experiment with one of these highly phosphorized proteids.

*Experiment 8.*—Therefore, four fowls were fed on polished rice and given a daily dose of 0.2 gram of dried nuclein. This is a very large quantity compared with the nuclein that would be naturally received in the food of a fowl. The nuclein was obtained from a leading pharmaceutical house in Manila.

*Group A:* Four fowls fed on polished rice plus 0.2 gram of nuclein daily.—One fowl developed neuritis in thirty-three days; one fowl developed neuritis in thirty-six days.

Two fowls were well after fifty-six days when the experiment was concluded.

As 2 fowls out of 4 developed neuritis, it is not believed that the nuclein used had any decided power to prevent polyneuritis gallinarum. Since the incubation period for the 2 fowls which did develop neuritis is perhaps slightly above the average, and since 2 fowls remained well at the end of fifty-six days, it can not be denied that there may have been a small amount of neuritis-preventing substance in the nuclein, a quantity sufficient to retard the outset of the disease. As will be stated later on, our work has led us to suspect that the neuritis-preventing principle may ultimately be found among the decomposition products of protein. It is possible that small quantities of such material may have been present in the nuclein. We have not made any further experiments with nuclein because the question as to whether or not nuclein was efficacious had no direct bearing on the main line of investigations we were pursuing.

Hulshoff-Pol<sup>(4)</sup> proved that a decoction of *katjang idjo* (*Phaseolus radiatus*) prevented and cured beriberi. It has been generally accepted in the Philippines that these beans, known here under the name of *mongos*, possess this property, and for a while mongos were supplied to the Philippine Scouts (native) as a part of their ration for the purpose of preventing beriberi. However, it was found difficult to obtain mongos

in sufficient quantity in the local market, they did not keep very well, and the Scouts did not like them as a steady article of diet. There are no such objections to the use of the ordinary white bean that constitutes a part of the army ration, but there was no information obtainable as to whether it would prevent beriberi. It seemed to us quite probable that the white bean would be just as efficacious in this respect as any other legume. Therefore, we tested these beans in the following experiment.

*Experiment 9.*—One kilogram of dried white beans was soaked overnight in distilled water, and the following day boiled for two hours, allowing the decoction to evaporate down to such a point that 1 liter of fluid remained. The cloudy liquid obtained was filtered until perfectly clear. This fluid was of a deep yellow color with a tendency to become opalescent on standing, and had a distinct odor of beans. It was preserved in the ice box with the addition of a slight quantity of chloroform. Ten cubic centimeters of the fluid represented the substances extracted by boiling water from 10 grams of beans. We then treated 1 kilogram of mongos in a precisely similar manner, obtaining from them a corresponding extract.

Nine fowls were now fed on polished rice. Five fowls received daily in addition 10 cubic centimeters of extract of beans, while the other 4 fowls received 10 cubic centimeters of extract of mongos. The result of this experiment is as follows:

*Group A:* Five fowls fed on polished rice plus 10 cubic centimeters of extract of beans daily.—All five fowls remained healthy at the end of sixty days when the experiment was discontinued.

*Group B:* Four fowls fed on polished rice plus 10 cubic centimeters of extract of mongos daily.—One fowl developed neuritis on the thirty-fifth day; the other three fowls remained well at the end of sixty days when the experiment was discontinued.

We do not believe this experiment to indicate that mongos will fail to prevent beriberi. On the contrary, we believe that they will prevent this disease. The extract of mongos as we prepared it was filtered until perfectly clear, and it is quite probable that we removed in this manner many of the substances which were present in Hulshoff-Pol's decoction. This part of the experiment, therefore, only demonstrates that the extract as we prepared it failed to confer complete protection. The important fact in this experiment is that the fowls receiving extract of beans were completely protected. Therefore, the ordinary white bean, must contain a neuritis-preventing principle.

While we do not wish to claim too much on the basis of a single experiment, we ourselves are convinced that the ordinary white bean will prove equally as efficacious as the mongo in the prevention of beriberi. This is a very important observation since it indicates that we may use these

beans as a preventive against beriberi in the rations of native troops, native prisoners, and others. Probably in actual practice the ordinary white bean may be even more efficacious than mongos, because beans are more savory and are more desired as an article of diet by all classes of men. This point must be borne in mind when prescribing for natives a diet consisting largely of rice. If the natives do not happen to care for mongos, or the other articles introduced into the ration for the purpose of preventing beriberi, they will not eat them, but will live on an almost exclusive diet of rice; but the man, native or white, who does not relish well cooked beans is hard to find, and it is believed that they would be generally eaten by persons who would refuse to eat mongos.

It is also quite possible that this observation will be of further assistance in identifying the beriberi-preventing principle. Extracts of beans and of rice polishings doubtless contain many substances peculiar to themselves, but we may find some substance, or a few substances, common to both of these extracts. If this should occur, it is probable that the neuritis-preventing principle will be found, or at least the search for it will be restricted to very narrow limits.

We have also performed some experiments in the course of which we evaporated the extract of rice polishings to dryness in a water bath at 100°C. This necessitated prolonged heating at this temperature and we found that the extracts so prepared had lost their efficacy. It has long been known that even a brief exposure to a temperature of 120°C. destroyed the neuritis-preventing substance and it is now shown that prolonged exposure to a temperature of 100°C. will also produce the same effect. It is possible that this is the reason why our decoction of mongos lost some of its power, and we would recommend, therefore, that no extract supposed to contain the neuritis-preventing principle should be boiled for more than one hour.

#### CONCLUSIONS.

We have made some progress in the identification of the neuritis-preventing substance contained in the extract of rice polishings prepared by the method described in our first paper. Of 1.34 per cent total solids contained in this extract, 0.03 per cent was ash. This we believe to be negligible since it consists entirely of inorganic constituents, chiefly of lime, magnesia, and potassium carbonate. We have tried salts of calcium, magnesium, and potassium and found them wanting. Nitrogenous matter comprises 0.04 per cent of the total solids. Of this only 0.02 per cent was present in the diffusate, which has been shown to contain the neuritis-preventing principle, and the remaining 0.02 per cent can be eliminated because it remained in the dialysate which failed to prevent neuritis. The 0.88 per cent sucrose is of no importance. Combining these unimportant substances and subtracting them from the 1.34

per cent of total solids, we find that there is only 0.4 per cent remaining. The neuritis-preventing principle must, therefore, be sought for in this 0.4 per cent of solid matter and must be a substance that is dialyzable, that is soluble in water, in 95 per cent alcohol, and in 0.3 per cent hydrochloric acid, which is easily decomposed by heat and which possesses a strong affinity for bone black. The same substance or a similar substance is also contained in a decoction of ordinary white beans. Bodies corresponding to this description are found among the decomposition products of the proteids. Therefore, it appears to us, that we have obtained sufficient information with regard to the nature of this body to attempt to identify it by the direct methods of chemical analysis. We have already begun experiments along these lines with the assistance of Mr. R. R. Williams, of the laboratory of organic chemistry, Bureau of Science, Manila, and expect to report them in the near future.

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# A STUDY OF ARNETH'S NUCLEAR CLASSIFICATION OF THE NEUTROPHILES IN HEALTHY ADULT MALES AND THE INFLUENCE THEREON OF RACE, COMPLEXION, AND TROPICAL RESIDENCE.<sup>1</sup>

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By WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.<sup>2</sup>

(*From the United States Army Board for the Study of Tropical Diseases as they  
Exist in the Philippine Islands.*)

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## INTRODUCTION.

In the quarterly report of the Board for September 30, 1910 (published in the *Military Surgeon* for February, 1911) there was a preliminary report upon some observations by the Board regarding the Arneth classification of the neutrophiles for Filipinos and for white men living in the Philippines. Since the original work a much larger series of cases has been studied, counts having been completed on 72 Americans and 50 natives. The earlier and the later observations were made independently by different members of the Board and the results of both series are practically identical. Therefore, it is safe to say that the personal equation, which might be a considerable factor in this kind of work, has been discounted in making up the final result. These examinations were originally undertaken as a part of the investigation into the influence of tropical light on blonds and brunettes, and the research was subsequently extended to natives among whom most interesting results have been obtained. As far as we can learn no work along this line has previously been undertaken in the Tropics.

## BRIEF DESCRIPTION OF ARNETH'S CLASSIFICATION.

A classification of polymorphonuclear neutrophiles based on the number of nuclei or nuclear fragments was proposed by Arneth in 1904.<sup>(1)</sup> He described

<sup>1</sup> Published by permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> Weston P. Chamberlain, major, Medical Corps, United States Army and Edward B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

5 main classes.<sup>3</sup> Class I has a single nucleus which may be round or of irregular shape. If the nucleus is round, the cell is then identical with Ehrlich's neutrophilic myelocyte<sup>(3)</sup> which is not found normally in the peripheral circulation. Class II includes the neutrophils with 2 nuclei or nuclear fragments. Class III has 3 nuclei or fragments and is the largest class in normal blood. Classes IV and V have respectively 4 and 5 nuclei or nuclear fragments. A fairly constant proportion between the different classes is found in normal blood. The "neutrophilic blood picture" as given by Arneth is for each one 100 polymorphonuclear leucocytes as follows:

Class I.	Class II.	Class III.	Class IV.	Class V.	Index (Arneth).	Index (Bushnell and Treuholtz).
5	35	41	17	2	40.0	60.5

Simon<sup>(3)</sup> gives the following normal range for each 100 neutrophils:

Class I.	Class II.	Class III.	Class IV.	Class V.
4-9	21-47	33-48	9-23	2-4

The so-called nuclear fragments seldom if ever represent separate nuclei, but only lobes of a polymorphous nucleus, the connecting nuclear substance being drawn out into a fine thread. The "index" is a standard for comparison of different pictures. Arneth adopted as an "index" the sum of classes I and II while Bushnell and Treuholtz selected the sum of classes I and II and one-half of class III.<sup>(13)(14)</sup>

The polymorphonuclear leucocyte is the active phagocytic cell of the blood stream and the corpuscles with 3 or 4 nuclear fragments are considered the adults and are thought to be most active as phagocytes and best fitted to protect the body against invading organisms. The superannuated cells represented by class V and the immature cells represented by classes I and II are less able to take up the defence of the body. Pottenger in a series of experiments found a gradual rise in phagocytic power from class I to class IV inclusive, and a decrease in class V.

When the first and second classes are increased above normal and the third and fourth are correspondingly decreased the condition is spoken of as a "shift or a drift to the left" while the reverse alteration is called a "shift to the right." Pottenger,<sup>(4)</sup> Klebs,<sup>(15)</sup> Kagan,<sup>(2)</sup> Minor and Ringer<sup>(13)</sup> and others have found a decided shift to the left in patients with marked lesions of tuberculosis and Kagan also found a less marked shift to the left in cases

<sup>3</sup> Arneth subdivided his 5 main classes into a number of smaller groups with distinctions depending upon the indentations and the character of the loops and lobes. These sub-groups seem to us to be an unnecessary and impractical refinement and moreover the number in each sub-division is too small to be of value unless 500 or 1,000 neutrophils are counted<sup>(6)</sup>. Such a procedure is very time-consuming and does not appear to us to promise compensating advantages.

of sepsis. Solis-Cohen and Strickler were not able to find any shift to the left in tuberculous patients at any stage of the disease although the polymorphonuclear cells were reduced in numbers.<sup>(6)</sup> Arneth considers a shift to the left an evidence of lowered resistance to the disease affecting the patient whose blood he is studying, as is indicated by the fact that when a tubercular patient improves the blood picture tends to return to the normal.<sup>(13)</sup>

#### OUR METHOD OF STAINING AND COUNTING.

Most of our counts were made with very thin smears stained with Wright's stain. A few were stained with hematoxylin and eosin after the method of Bushnell and Treuholtz. This method gave excellent pictures but did not seem to offer sufficient advantages to compensate for the trouble of making a second stain for the differential count. Whatever staining method is used, it is important that smears be thin. We have tried the technique of Wiedenreich, but without success.<sup>(16)</sup>

Even in a well-spread and well-stained slide there will always be an uncertainty as to the group in which some nuclei should be classified. Pottenger considers that these doubtful cells constitute 12 per cent of the total when Wright's stain is used. To obtain uniform results, we adopted the following rules in counting:

(1) Nuclear masses connected by a distinct isthmus were counted as 1 nucleus, while masses connected by only a thread were counted as 2 nuclei.

(2) Nuclear masses clearly superimposed were considered as separate nuclei, but where the superposition was not distinct the body was considered a single nucleus.

(3) In all instances when there was doubt as to whether a cell should be grouped in one or the other of two classes, it was always placed in the *higher* class.

By a careful adherence to rule 3 we have avoided the possibility of producing an artificial shift to the left. If all doubtful cells had been recorded alternately, the first in a lower and the second in a higher class, the shift to the left which we found for bloods in the Tropics would have been even more pronounced than we now claim.

In our work we enumerated for differential counts 200 cells for each individual. For the Arneth work we counted 200 cells each from a part of the men and 100 each from the remainder. While an enumeration of 100 cells for Arneth work and of 200 cells for differential counts may in a few instances lead to slight errors for the individual, it is believed that it is ample to give accurate average results such as we were seeking in our investigation.

The following table indicates how close an agreement in the results for both differential and Arneth counts was obtained by our two independent observers working at different times.

TABLE I.—*Agreement of differential and Arneth counts as made by two independent observers in the Philippines.*

Observer.	Men observed.		Differential counts, per cent.							Arneth's classification, per cent.					Index (Arneth).	Index (Bushnell and Treuboltz)
	Race.	Number.	Polynuclears.	Eosinophiles.	Small lymphocytes.	Large lymphocytes.	Transitionals.	Mast cells.	I.	II.	III.	IV.	V.			
A	Americans_____	22	56.4	5.1	30.0	4.1	3.5	0.9	13.4	34.8	39.0	11.3	1.5	48.2	67.7	
B	Americans_____	50	57.0	3.2	32.4	5.0	1.7	0.7	13.2	32.0	36.3	17.3	2.1	45.2	63.3	
A	Filipinos. _____	21	48.1	13.6	28.1	6.2	3.2	0.8	28.1	41.2	24.7	5.3	0.7	69.3	81.6	
B	Filipinos. _____	29	55.1	8.6	31.2	3.4	1.1	0.6	27.0	36.3	26.6	9.1	1.0	63.3	76.6	

It will be observed that the Arneth index of Observer A is slightly higher for Americans than that of Observer B and that the same is true for the observations on Filipinos, so there is complete agreement between the two observers as regards the finding of a marked shift to the left for natives. The same remarks are true when the Arneth counts are compared on the basis of the index of Bushnell and Treuholtz.

THE INFLUENCE OF RACE AND TROPICAL RESIDENCE ON THE DIFFERENTIAL AND THE ARNETH COUNT.

The appended tables (Nos. V and VI) give the individual data for our series of 122 counts. When divided according to race, American or Filipino, the white cell count per cubic millimeter was found within normal limits in both races,<sup>(7)</sup> averaging a little higher for the Filipinos, 9,248 as compared with 7,304 for Americans. The average differential leucocyte count showed for both races the characteristic changes found by this Board,<sup>(9)</sup> <sup>(10)</sup> and by others,<sup>(11)</sup> <sup>(12)</sup> in the blood of Filipinos and of white men resident in the Philippines, namely, a decreased polymorphonuclear count associated with an increased percentage of small lymphocytes and, for the natives, an increase in the eosinophilic cells due in the vast majority of cases to infestation with intestinal parasites. The reduction in polymorphonuclear neutrophiles was slightly greater for natives, who had 52 per cent of these cells as compared with 56 per cent for Americans.

When the Arneth count came to be considered very marked differences were found between the averages for the two races. There was evident a slight shift to the left in the average count for white men as compared with the standard recognized by most authorities in Europe and America.<sup>4</sup> Since we have not counted for comparison any extensive series of blood

<sup>4</sup> These normal "standards" vary considerably with the writer, and we believe this variation is in part due to the fact that most observers have counted too small a series of normal cases.



smears from men residing in America, we are unable to state whether this slight drift to the left is due to climatic influence or to our own personal equations in enumerating. For the Filipinos we found a very decided shift to the left and are sure that this represented an actual and wide departure from the Caucasian average, because we have as a standard for comparison our series made simultaneously on white men in the same locality.

Our average results for differential and Arneth counts for the two races, compared with several writers' estimates of the normal are shown in Table II. For the 72 Americans the average length of the *present tour* of tropical duty was 14.6 months and the average total tropical service 28.7 months.

TABLE II.—*Arneth counts on healthy Americans in the Philippines and on healthy Filipinos, contrasted with normal counts in Europe and America.*

	White cells per cu. mm.	Differential counts, per cent.					Arneth's classification, per cent.					Index (Arneth).	Index (Bushnell and Treuholtz).
		Polynuclears.	Eosinophiles.	Small lymphocytes.	Large lymphocytes. <sup>a</sup>	Mast cells.	I.	II.	III.	IV.	V.		
Normal (Simon) -----	3,000	60	1	20	1	0.2	4	21	33	9	2	25	}
	to	to	to	to	to	to	to	to	to	to	to	to	
Normal in Europe (Arneth) -----	10,000	70	4	30	6	1.0	9	47	48	23	4	56	}
Normal in United States (Kagan) -----							5	35	41	17	2	40.0	60.5
Normal (Buchanan and Williams) <sup>b</sup> -----	5,000	70	0.5	20	3	0.5	8	36	42	13	1	44.0	65.0
	to	to	to	to	to								
Average for 72 healthy Americans in Philippine Islands -----	10,000	90	4	30	6								
Average for 50 healthy Filipinos -----													
	7,304	56.8	3.8	31.7	6.9	0.8	13.3	32.9	37.2	14.6	2.0	46.2	64.8
	9,248	52.2	10.6	29.9	6.6	0.7	27.5	38.3	25.8	7.5	0.9	65.8	78.7

<sup>a</sup> With the large lymphocytes have been classed the transitional forms, following the grouping of Simon.

<sup>b</sup> The average white and differential counts given in this line are from R. J. M. Buchanan, *Blood in Health and Disease* (1909). The Arneth averages are from 100 counts on 55 individuals in the United States by W. W. Williams in *Colorado Medicine* (1911), 8, 175.

*From the tables it is evident that there is a very marked shift to the left in the Arneth count for Filipinos and apparently a slight movement in the same direction for Americans resident in the Philippine Islands.*

#### THE ARNETH INDEX IN THE TWO RACES.

The index, referred to in an earlier part of this paper, is very useful to give at a glance a basis of comparison between different Arneth counts.

The more marked the shift to the left, the higher will be the index. For our American series the index adopted by Arneth (sum of classes I and II) was 46.2 which is but a little higher than the index of 40 found by Arneth for normal individuals in Europe. For the Filipinos of our series the index is much elevated, averaging 65.8.

Using the index adopted by Bushnell and Treuholtz (sum of classes I and II and one-half of class III) there also appears a decided elevation for the Filipinos, average 78.7, as compared with 64.8 for Americans resident in the Philippines, but the differences are not as great as when the index adopted by Arneth is employed.

THE INFLUENCE OF THE COMPLEXION OF WHITE MEN ON THEIR ARNETH COUNT IN THE PHILIPPINES.

We have for eighteen months been at work on the influence of the Philippine climate on soldiers of the blond and the brunette types of complexion who have served a year or more in the Islands. By blond we mean a man with light brown, sandy, red, or flaxen hair, blue or gray eyes, and a light or ruddy complexion; by brunette one with dark brown or black hair, brown or black eyes, and a dark complexion. Men in whom eyes, hair, and complexion do not *all* conform to the same type are classed as mixed types and excluded from consideration. The blood counts considered below are from men who were pronounced specimens of the type they represent.

TABLE III.—*Leucocyte count, differential count and Arneth's count on 28 blonds and 28 brunettes resident in the Philippines.*

Complexion type.	White cells per cubic millimeter.	Differential counts, per cent.						Arneth's classification, per cent.					Index (Arneth).	Index (Bushnell and Treuholtz).
		Polynuclears.	Eosinophiles.	Small lymphocytes.	Large lymphocytes.	Transitionals.	Mast cells.	I.	II.	III.	IV.	V.		
Blond -----	7,077	55.5	4.3	33.0	4.5	1.9	0.8	11.5	31.6	38.2	16.2	2.1	43.1	62.2
Brunette ----	7,888	60.2	3.5	29.0	4.5	2.1	0.7	14.5	34.5	35.7	13.6	1.8	49.0	66.8

The length of the present tour of tropical service averaged 16.5 months for the blonds and 16.2 for the brunettes. If previous tours of tropical service are added then the average total tropical service was 29.1 months for the blonds and 36.0 months for the brunettes.

It will be observed that the proportion of the polymorphonuclear leucocytes (phagocytic cells) is slightly less for the blonds (55.5 per cent as compared with 60.2), while the brunettes show a somewhat higher index for the Arneth count, whether reckoned by the method of Arneth or that of Bushnell and Treuholtz. We believe that these differences are unimportant and due to the inherent error attaching to such a small

series of cases. Some authors have considered that blonds are less well able to stand the influence of a tropical climate. As far as our small series of observations is concerned, we do not think this view is supported; in fact the higher Arneth indexes for brunettes, if found to be constant in larger series, might indicate the reverse condition.

THE POSSIBLE SIGNIFICANCE OF LOW POLYMORPHONUCLEAR COUNTS AND HIGH ARNETH INDEXES IN FILIPINOS.

In estimating the significance of the blood counts which we have found in Filipinos it is necessary to consider the four factors discussed below.

1. *Low polymorphonuclear count in Filipinos.*—That the polymorphonuclear cells of Filipinos and of Americans long resident in the Philippines are reduced below the minimum point considered normal for Americans and Europeans at home seems quite well settled. Some results found in healthy persons in the Philippines are shown in the following table.

TABLE IV.—*Reduction in polymorphonuclear neutrophiles found in the Philippines.*

Observers.	Race.	Number observed.	Residences in Philippine Islands.	Polynuclears.	Eosinophiles.	Small lymphocytes.	Large lymphocytes. <sup>e</sup>	Mast cells.
Wickline (12) _____	Americans <sup>a</sup>	104	Batangas..	54.9	5.1	33.4	6.1	0.5
Guerrero and Sevilla (11) ____	Filipinos ____	129	Taytay ____	51.6	11.2	34.5	4.1	0.2
This Board (10) _____	Americans <sup>b</sup>	115	Various ____	58.7	3.6	32.6	4.6	0.5
This Board (9) _____	Igorots <sup>c</sup>	40	Baguio ____	46.9	8.9	37.2	5.7	0.4
This Board _____	Americans <sup>d</sup>	72	Various ____	56.8	3.8	31.7	6.9	0.8
Do _____	Filipinos <sup>e</sup>	50	____do____	52.2	10.6	29.9	6.6	0.7

<sup>a</sup> These were all soldiers who had served continuously in the Philippines over 18 months at the time the counts were made.

<sup>b</sup> All the members of this group were soldiers who had been in the Philippines over a year.

<sup>c</sup> All of this group were adult males.

<sup>d</sup> All of these were soldiers with an average of 14 months' continuous Philippine service.

<sup>e</sup> Includes transitional forms.

In all of the counts made by ourselves care has been taken to count back and forth completely across the slide to avoid obtaining an undue number of small lymphocytes which are liable to be more numerous in the central portion of the smear than at the borders.

That these low polymorphonuclear and high lymphocyte counts for Americans developed gradually after residence in the Philippines and were not present on their arrival in the Islands has been shown by Wickline.<sup>(12)</sup>

2. *The cells of the body which are phagocytic.*—It is generally accepted that the small lymphocytes have no phagocytic power. Buchanan says that the

"coarse eosinophiles are actively amoeboid and to a certain extent phagocytic"(7), while Kanthack and Hardy consider that they never act in this way.(8) Wesbrook once observed phagocytosis by these cells, but considers it extremely rare.(8) It has also been stated that virulent living bacteria act in a negatively chemiotactic manner on eosinophiles.(5) Buchanan considers the large mononuclears to act as phagocytes,(7) but Kanthack and Hardy believe that only in case of feebly virulent bacteria are they capable of immediate action. That certain fixed cells, notably endothelial cells, have phagocytic power is generally accepted, but the extent and manner of their action is not very thoroughly understood.

As far as the blood is concerned the chief phagocytic cell is the polymorphonuclear neutrophile, the "microphage" of Metchnikoff. This is the only blood cell which is generally recognized as being able to engulf and destroy bacteria. Its importance in the production of immunity was overshadowed for a time by the work of Ehrlich, but has again been brought into prominence by the researches of Wright.

Cabot says, "*It would appear that the degree of health in persons not organically diseased might perhaps prove to vary directly with the percentage of polymorphonuclear cells in the blood.*"

3. *Influence on phagocytosis of a high Arneth index.*—As before stated, Arneth considers that classes I and II of his classification represent the immature leucocytes and that they are less able to protect the body than are the cells with three or four nuclear fragments. Pottenger(4) reports that the phagocytic power of the leucocytes for staphylococci gradually rises from class I to class IV inclusive and diminishes for class V. On the other hand, Buchanan, using cocci, could not detect any relation between the number of nuclear divisions and the number of bacteria engulfed by the cell.

Turning from experimental researches to clinical observations, it will be found that nearly all of the work with the Arneth classification has been done on patients suffering from tuberculosis. It seems quite generally accepted that a marked shift to the left indicates lowered resistance to that disease. In other words, a high Arneth index goes hand in hand with a low resistance or with a high degree of toxic and bacterial absorption which is leading to the destruction of the actively phagocytic cells (classes III and IV). By a large number of examinations in various infectious diseases, Arneth has demonstrated a direct relationship between the blood picture and the course of the disease. The picture is therefore considered an index of the protective efforts of the body against infections.(15)

It seems to us reasonable to conclude from the foregoing that a bad Arneth blood picture, if found habitually in the apparently normal individuals of a race, probably indicates a diminished resistance on the part of that race to various infections. This conclusion is merely offered as an hypothesis.

4. *Leucocytometry in the Filipinos.*—We have not been able to find

much evidence as to the number of white cells per cubic millimeter in the blood of healthy natives. Our own work on 29 adult male Filipinos gave an average count of 9,248. This may seem a trifle high, but it is at least well within the normal upper limit of 10,000 given by Simon, Buchanan and Cabot.

It may be mentioned that our average of 9,248 agrees closely with the average of 9,000 given by Castellani and Chalmers for adult male Bengalese in India.

*Summary.*—After a consideration of the above four sections it will be evident that in our series of Filipino bloods there is: First, an absolute number of white cells within normal limits; second, a markedly low relative proportion of polymorphonuclear neutrophiles; and third, an abnormally high percentage of the neutrophilic elements which fall in classes I and II of Arneth and which are supposed to be deficient in phagocytic power. Therefore, in the Filipino blood there is both a relative and an absolute reduction in the phagocytes, the cells which, with the aid of opsonins, are concerned in destroying bacterial invaders.

If this state of things is general in tropical races, it may be a visible indication of the lowered resistance of such peoples to certain newly introduced maladies and to some epidemic tropical diseases which generally cause a higher mortality among natives than is experienced among Caucasians. In the first class of diseases may be mentioned measles, leprosy, syphilis, and tuberculosis, and in the second class plague and cholera. Apparently the natives of the Philippines have a good resistance to infections with staphylococci and streptococci, and this clinical fact may be related to the observations of Buchanan who could find no relationship between the degree of nuclear subdivision and the number of cocci engulfed by the neutrophilic cells.

#### POSSIBLE INFLUENCE OF TROPICAL CLIMATE.

Whether the reduction we have found in the phagocytic elements of the blood may be the result of a tropical climate *per se* is an interesting subject for speculation and for future study. About a year ago we suggested<sup>(9)</sup> that the low polymorphonuclear count in natives and white men in the Philippines might indicate lowered resistance and be due to tropical conditions. The work of Wickline showing that the decrease of polymorphonuclear elements becomes progressively more marked as the length of residence in the Philippines increases, is suggestive that the change is due to the climate. Our recent work with the Arneth classification points in the same direction, since the index for white men who had lived over a year in the Islands is a little higher than has been found normal in temperate climates by most observers. On account of the many complicating factors, three of which are mentioned below, it will be extremely difficult to establish a direct relationship between climate and diminished phagocytic power.

In the case of the Filipinos in our series a possible influence of tuberculosis should be borne in mind. All of the counts were made on apparently healthy laborers, but no physical examinations were made to exclude latent or incipient tuberculosis as a cause of a high Arneth index. Although tuberculosis is widespread among the Filipinos, we do not believe that it is so prevalent as markedly to raise the average Arneth index of a series of 50 men engaged in daily labor and to all outward appearances in perfect health.

Intestinal parasites greatly modify the blood findings in Filipinos and are responsible for the eosinophilia almost invariably met with. It is impossible at present to state whether infestation with intestinal worms produces a modification in the Arneth index.

Diet is a third factor which conceivably might influence a blood picture. The food of the Filipino consists largely of rice and is low in nitrogenous components. It would be of much interest to make a series of Arneth counts on Japanese and northern Chinese, people who dwell in a temperate climate yet have dietary habits similar to those of tropical races.

#### CONCLUSIONS.

1. Both Filipinos and Americans residing more than a year in the Philippines had a normal average number of white cells per cubic millimeter.

2. In both races the percentage of polymorphonuclear neutrophiles was much decreased below the minimum considered normal for white men in temperate regions.

3. Probably the polymorphonuclear neutrophiles are the only actively phagocytic cells in the circulating blood.

4. The average Arneth picture showed a marked shift to the left in the case of Filipinos and a slight drift in the same direction for Americans resident more than a year in the Philippines.

5. A shift to the left in the Arneth count probably indicates a diminution in the phagocytic power of the blood in question.

6. From the first five conclusions it will be apparent that the Filipinos show an actual absolute reduction in the number of polymorphonuclear neutrophiles (phagocytes), and that of this reduced number an abnormally large proportion are deficient in phagocytic power. In other words, the Filipino has absolutely fewer efficient phagocytes than are found among white men either in the Philippines or at home.

7. This reduction in circulating phagocytic cells may be a visible indication of a lowered resistance to infections on the part of native races.

8. No material differences in the differential count or the Arneth picture were observed between two groups of American soldiers, one group consisting of 28 pronounced blonds and the other group of 28 pronounced brunettes.

TABLE V.—Differential and Arneth counts on the blood of Americans residing in the Philippines.

No.	Birthplace.	Residence.	Age.	Tropical service, months.		Complexion. <sup>a</sup>	Red cells.	Hb.	White cells.	Polynuclears.	Large lymphocytes.	Transitional.	Small lymphocytes.	Eosinophiles.	Mast cell.	Arneth classification.				
				Present tour.	Total.											I.	II.	III.	IV.	V.
1	New York	New York	24	12	12	M.	-----	P. cl.	6,700	40.0	6.0	4.0	48.5	1.5	0.0	7.5	38.5	37.5	15.0	1.5
2	Pennsylvania	Pennsylvania	33	22	52	M.	-----	95	5,600	43.0	4.0	2.0	48.0	2.0	1.0	9.0	28.0	48.0	13.0	2.0
3	New York	Pennsylvania	32	6	36	Bl.	-----	98	6,300	60.0	6.5	2.0	29.5	1.0	1.0	8.5	31.0	39.5	19.0	2.0
4	Alabama	Georgia	28	13	13	M.	-----	98	6,800	49.0	6.5	3.0	38.0	3.0	0.5	10.0	33.0	36.5	19.5	1.0
5	Missouri	Arkansas	25	11	11	Br.	-----	92	8,500	58.0	7.0	1.5	30.0	3.0	0.5	19.5	35.0	35.5	9.5	0.5
6	Minnesota	Minnesota	23	1	1	Br.	-----	90	8,200	56.7	7.3	1.0	34.0	0.0	1.0	29.0	35.0	27.0	9.0	0.0
7	New York	Nebraska	45	2	13	Br.	-----	98	9,200	67.0	4.0	2.5	23.5	3.0	0.0	18.5	37.5	35.5	8.5	0.0
8	Kansas	District of Columbia.	25	1	3	Bl.	-----	85	5,600	60.0	4.0	2.0	32.0	0.5	1.5	11.5	31.5	40.0	16.0	1.0
9	Pennsylvania	Pennsylvania	32	1	1	Br.	-----	97	9,000	58.0	3.0	2.0	35.5	1.5	0.0	11.5	29.5	36.0	18.0	5.0
10	Missouri	Missouri	25	2	2	Bl.	-----	90	6,400	45.5	7.0	5.5	40.5	0.5	1.0	32.0	28.0	34.0	4.0	2.0
11	Missouri	Missouri	22	16	16	Bl.	4,760,000	95	5,500	44.0	4.5	3.5	41.5	6.5	0.0	11.0	23.0	44.0	20.0	2.0
12	Montana	Montana	23	18	18	Bl.	4,200,000	83	8,200	55.5	1.5	0.5	35.5	6.0	1.0	12.0	25.0	42.0	19.0	2.0
13	Indiana	Nebraska	32	17	17	Br.	5,000,000	92	6,900	64.5	5.0	1.5	27.5	1.0	0.5	12.0	34.0	39.0	14.0	1.0
14	Illinois	Illinois	24	18	18	Bl.	4,200,000	80	6,400	59.0	5.0	2.5	33.0	0.5	0.0	5.0	19.0	44.0	28.0	4.0
15	Texas	Texas	26	18	18	Br.	4,900,000	95	8,200	55.0	4.5	1.5	30.0	8.0	1.0	7.0	25.0	40.0	24.0	4.0
16	Wisconsin	Nebraska	39	16	49	Bl.	4,640,000	85	8,700	70.5	5.0	1.5	19.5	1.5	2.0	9.0	26.0	42.5	18.0	4.5
17	Pennsylvania	Iowa	35	16	16	Bl.	4,800,000	90	6,500	57.0	4.5	3.0	30.0	5.0	0.5	11.0	21.0	39.0	22.0	7.0
18	Ohio	Ohio	45	16	48	Br.	4,600,000	90	6,900	65.5	5.5	1.5	25.5	1.0	1.0	16.0	35.0	29.0	18.0	2.0
19	Wisconsin	Wisconsin	45	16	82	Br.	4,800,000	92	7,300	68.5	4.0	2.0	23.0	2.0	0.5	14.0	30.0	42.0	13.0	1.0
20	Europe	Europe	24	16	16	Bl.	4,640,000	95	7,500	61.0	4.0	1.5	31.0	0.5	2.0	13.0	35.0	33.0	16.0	3.0
21	Illinois	Illinois	29	16	16	Br.	4,900,000	92	7,200	70.0	4.5	2.0	23.0	0.5	0.0	24.0	29.0	34.0	13.0	0.0
22	Michigan	Michigan	24	16	16	Bl.	4,800,000	90	6,100	53.0	5.0	1.0	38.5	1.5	1.0	22.0	34.0	29.0	14.0	1.0

<sup>a</sup> Bl. means blond, Br. means brunette, M. means mixed type of complexion.

TABLE V.—*Differential and Arneeth counts on the blood of Americans residing in the Philippines—Continued.*

No.	Birthplace.	Residence.	Age.	Tropical service, months.		Complexion. <sup>a</sup>	Red cells.	Hb.	White cells.	Polynuclears.	Large lymphocytes.	Transitional forms.	Small lymphocytes.	Eosinophiles.	Mast cell.	Arneeth classification.				
				Present tour.	Total.											I.	II.	III.	IV.	V.
								<i>P. ct.</i>												
23	Rhode Island	Massachusetts	27	16	16	Br.	4,800,000	92	10,000	59.5	4.5	1.0	28.0	5.5	1.5	26.0	39.0	25.0	8.0	2.0
24	Illinois	Illinois	22	16	16	Bl.	4,800,000	80	7,700	49.5	5.5	1.5	31.0	12.5	0.0	16.0	27.0	38.0	18.0	1.0
25	Missouri	Missouri	27	16	16	Bl.	4,200,000	85	7,500	63.4	4.1	1.5	29.5	0.5	1.0	17.0	32.0	33.0	16.0	2.0
26	Kentucky	Kentucky	20	16	16	Br.	4,640,000	90	7,800	58.0	7.0	3.0	31.5	0.5	0.0	13.0	31.0	37.0	18.0	1.0
27	New York	New York	28	16	16	Br.	4,440,000	82	7,900	57.5	5.5	1.0	30.0	6.0	0.0	14.0	36.0	32.0	16.0	2.0
28	Michigan	Colorado	23	16	16	Bl.	4,560,000	85	7,300	69.0	5.5	2.5	19.0	3.5	0.5	10.0	36.0	36.0	17.0	1.0
29	Indiana	Indiana	34	16	18	Br.	4,200,000	80	7,600	67.0	5.0	1.5	24.5	1.5	0.5	13.0	24.0	45.0	16.0	2.0
30	Massachusetts	Massachusetts	30	17	17	Br.	4,640,000	85	7,400	57.5	4.5	2.0	34.5	1.5	0.0	12.0	47.0	32.0	9.0	0.0
31	Tennessee	Washington	22	16	16	Bl.	4,460,000	85	6,700	43.5	9.5	2.0	40.5	3.5	1.0	6.0	31.0	42.0	18.0	3.0
32	Europe	Iowa	28	16	43	Bl.	4,200,000	90	5,000	47.0	3.5	1.0	48.5	0.0	0.0	4.0	24.0	43.0	27.0	2.0
33	Massachusetts	Massachusetts	29	16	61	Bl.	2,490,000	80	7,400	56.0	7.0	1.5	32.5	2.5	0.5	11.0	21.0	33.0	28.0	7.0
34	Europe	Europe	23	16	16	Br.	4,960,000	95	7,900	58.5	6.0	0.5	33.0	1.5	0.5	10.0	36.0	36.0	14.0	4.0
35	Europe	Utah	23	16	16	Br.	5,200,000	90	6,500	60.5	6.0	1.5	27.0	4.5	0.5	7.0	27.0	28.0	33.0	5.0
36	Europe	South Dakota	23	16	16	Bl.	4,440,000	80	8,500	45.0	5.5	0.5	39.0	8.0	2.0	23.0	23.0	35.0	17.0	2.0
37	Europe	Europe	27	16	16	Bl.	4,300,000	88	7,000	50.0	4.5	1.0	33.5	10.5	0.5	7.0	30.0	36.0	24.0	3.0
38	Europe	Minnesota	36	16	52	Bl.	4,840,000	92	8,300	64.5	5.0	1.0	26.0	2.5	1.0	9.0	29.0	41.0	20.0	1.0
39	Massachusetts	Massachusetts	30	24	42	Bl.	4,320,000	85	4,200	35.5	4.0	1.5	50.5	8.5	0.0	9.0	35.0	40.0	13.0	3.0
40	District of Columbia.	Arizona	18	16	16	Bl.	5,000,000	85	7,700	42.0	3.0	2.5	49.5	2.0	1.0	15.0	34.0	40.0	11.0	0.0
41	New York	New York	34	16	42	Br.	4,760,000	85	10,700	66.5	2.5	1.5	29.0	0.5	0.0	41.0	44.0	12.0	3.0	0.0
42	California	Missouri	22	16	16	Bl.	4,452,000	87	8,200	71.5	1.5	0.5	22.0	2.5	2.0	9.0	40.0	29.0	19.0	3.0
43	California	California	23	24	24	Br.	5,000,000	90	5,900	60.0	4.0	1.5	29.0	4.5	1.0	6.0	27.0	46.0	13.0	2.0
44	Texas	Texas	36	16	40	Br.	4,690,000	93	7,500	63.5	5.5	1.5	28.0	0.5	1.0	12.0	37.0	39.0	10.0	2.0
45	North Dakota	North Dakota	27	24	24	Br.	5,200,000	95	7,300	50.0	3.0	1.5	38.0	7.0	0.5	8.0	40.0	38.0	13.0	1.0

<sup>a</sup> Bl. means blond, Br. means brunette, M. means mixed type of complexion.



46	Missouri	33	16	64	Br.	4,710,000	90	7,100	46.0	7.0	1.0	39.0	6.0	1.0	8.0	42.0	32.0	14.0	4.0
47	Europe	21	16	16	Bl.	4,480,000	84	6,200	54.5	7.5	1.0	34.5	2.0	0.5	4.0	29.0	42.0	23.0	2.0
48	Europe	39	16	41	Br.	4,840,000	95	9,000	65.5	5.0	1.5	22.0	3.0	3.0	9.0	33.9	37.0	16.0	5.0
49	Missouri	30	16	76	Bl.	4,600,000	92	8,600	61.0	3.5	0.5	27.0	7.5	0.5	21.0	48.0	26.0	5.0	0.0
50	Europe	29	16	40	Br.	4,640,000	90	5,500	66.5	5.5	0.0	24.5	3.0	0.5	8.0	38.0	40.0	12.0	2.0
51	New York	30	6	38	Br.				62.0	8.0	4.0	23.0	2.0	1.0	3.0	20.0	48.0	23.0	6.0
52	Canada	40	15	51	Bl.				62.0	13.0	5.0	17.0	3.0	0.0	10.0	34.0	39.0	15.0	2.0
53	Missouri	19	6	6	M.				66.0	6.5	1.5	25.5	0.5	0.0	5.0	16.0	50.0	24.0	5.0
54	Illinois	28	7	7	M.				54.0	2.0	8.0	26.0	8.0	2.0	8.0	28.0	45.0	17.0	2.0
55	Virginia	31	4	18	Br.				58.5	5.5	2.5	29.0	3.0	1.5	26.0	45.0	23.0	5.0	1.0
56	Texas	24	6	18	Br.				60.0	2.0	2.0	29.0	5.5	1.5	12.0	37.0	35.0	15.0	1.0
57	Michigan	29	14	74	Br.				68.5	5.0	2.0	23.5	0.0	1.0	16.0	46.0	30.0	7.0	1.0
58	New York	23	22	22	Bl.				54.5	3.0	3.5	34.5	3.0	1.5	6.0	42.0	41.0	9.0	2.0
59	Arkansas	25	8	8	Br.				30.0	3.0	3.0	42.5	21.5	0.0	18.0	39.0	37.0	6.0	0.0
60	United States	40	12	12	M.				43.5	11.0	5.0	36.0	3.0	1.5	16.0	38.0	35.0	9.0	2.0
61	Pennsylvania	25	15	34	Br.	5,000,000	80	8,000	61.0	3.0	2.0	30.5	3.5	0.0	17.0	40.0	32.0	11.0	0.0
62	Europe	25	15	34	Br.	5,800,000	85	7,200	58.0	1.5	7.0	31.5	2.0	0.0	15.0	24.0	41.0	17.0	3.0
63	Pennsylvania	23	16	36	Br.	5,600,000	80	7,800	50.0	3.0	3.5	39.5	3.5	0.5	16.0	39.0	30.0	13.0	2.0
64	Pennsylvania	27	16	36	Br.	5,200,000	95	6,000	46.5	3.5	3.5	39.5	6.5	0.5	18.0	31.0	43.0	8.0	0.0
65	Virginia	27	16	36	Br.	4,400,000	80	8,000	58.0	2.0	4.0	32.5	2.5	1.0	12.0	40.0	33.0	14.0	1.0
66	Illinois	28	15	34	Bl.	6,000,000	85	7,200	68.5	2.0	1.5	18.0	9.0	1.0	14.0	51.0	32.0	2.0	1.0
67	Indiana	24	15	31	Bl.	4,800,000	100	5,600	56.0	2.0	2.0	33.5	6.0	0.5	5.0	27.0	51.0	15.0	2.0
68	New York	25	16	16	Bl.	5,200,000	80	7,000	60.0	1.0	1.5	33.5	3.5	0.5	12.0	45.0	40.0	3.0	0.0
69	Iowa	20	15	31	Bl.	4,800,000	85	7,200	50.0	1.5	5.0	41.5	1.0	1.0	16.0	37.0	38.0	9.0	0.0
70	Ohio	30	15	64	Bl.	5,200,000	90	7,800	50.0	5.0	1.5	35.0	7.0	1.5	17.0	30.0	44.0	9.0	0.0
71	Kentucky	38	13	97	Br.	6,440,000	90	9,100	56.0	2.5	3.0	24.0	13.5	1.0	17.0	31.0	45.0	7.0	0.0
72	Europe	42	13	76	Br.	5,336,000	85	5,900	69.0	4.0	5.0	15.0	4.0	3.0	16.0	26.0	46.0	10.0	2.0
Average			14.6	28.7		4,767,000	89	7,304	56.8	4.7	2.2	31.7	3.8	0.8	13.3	32.9	37.2	14.6	2.0

TABLE VI.—*Differential and Arneth counts on the blood of Filipinos.*

Number.	Age.	Hb.	White cells.	Polynuclears.	Small lymphocytes.	Large lymphocytes.	Transitional.	Eosinophiles.	Mast cell.	Arneth classification.				
										I.	II.	III.	IV.	V.
1	17	<i>P. ct.</i> 90	8,900	51.5	36.5	4.5	1.5	5.0	1.0	14	38	36	10	2
2	22	90	9,600	57.0	21.5	5.5	1.5	14.0	0.5	21	30	31	15	3
3	19	94	9,700	52.5	33.5	3.5	0.5	9.5	0.5	29	32	31	6	2
4	29	92	9,800	64.5	25.5	1.5	2.0	6.0	0.5	30	32	29	9	0
5	24	85	10,800	75.5	12.5	2.0	2.5	7.5	0.0	24	35	30	10	1
6	30	87	7,900	72.0	15.5	1.5	1.0	10.0	0.0	20	33	28	16	3
7	33	95	12,800	58.5	32.5	3.5	1.0	3.0	1.5	33	32	26	6	3
8	23	93	9,900	48.5	31.0	4.0	0.5	15.5	0.5	39	38	14	7	2
9	24	85	7,500	66.5	24.0	5.0	2.5	2.0	0.0	21	35	37	5	2
10	37	86	10,600	50.5	34.5	5.5	2.0	6.5	1.0	20	31	31	16	2
11	23	95	11,000	63.0	27.5	1.0	0.0	7.0	1.5	30	31	25	14	0
12	30	88	10,400	46.0	31.5	3.0	1.0	17.5	1.0	35	44	15	6	0
13	17	95	11,500	61.0	26.5	2.5	1.0	7.0	2.0	17	39	33	10	1
14	27	94	8,600	44.0	43.5	5.0	1.5	5.0	1.0	22	44	23	10	1
15	38	96	11,200	62.5	23.5	6.5	0.5	6.5	0.5	33	36	21	10	0
16	32	98	8,000	42.0	42.0	5.0	0.5	10.0	0.5	24	34	32	10	0
17	30	99	8,400	55.0	30.0	4.0	1.0	9.0	1.0	35	40	22	3	0
18	36	90	7,300	60.0	27.5	5.5	1.5	5.0	0.5	23	41	30	6	0
19	36	93	9,300	67.5	25.5	2.0	1.0	2.5	1.5	33	33	28	5	1
20	24	95	8,400	51.5	30.5	2.5	0.0	15.5	0.0	22	41	28	9	0
21	17	92	11,100	41.5	39.5	6.5	1.5	10.0	1.0	22	25	32	19	2
22	25	100	8,700	46.0	43.0	2.5	0.0	8.5	0.0	33	36	23	8	0
23	22	90	8,300	33.0	52.0	0.5	1.0	13.0	0.5	21	33	35	9	2
24	24	93	5,500	50.0	38.0	2.0	1.0	9.0	0.0	42	42	12	4	0
25	36	99	7,900	42.5	38.0	5.0	1.5	12.5	0.5	42	38	15	5	0
26	36	97	9,900	60.5	28.0	2.0	0.5	9.0	0.0	29	43	20	8	0
27	22	98	10,100	41.0	42.0	0.5	0.5	16.0	0.0	24	37	29	9	1
28	43	99	6,900	64.5	25.5	3.5	1.5	5.0	0.0	14	35	36	14	1
29	45	94	8,200	70.5	23.5	1.5	0.5	3.5	0.5	32	44	18	6	0
30	-----	-----	-----	50.0	33.0	3.5	6.0	7.0	0.5	28	40	30	1	1
31	-----	-----	-----	59.5	17.0	3.5	3.5	14.5	2.0	24	46	28	2	0
32	-----	-----	-----	59.0	26.5	5.0	2.0	6.5	1.0	28	45	21	5	1
33	-----	-----	-----	47.5	33.5	3.5	3.5	11.5	0.5	25	40	31	4	0
34	-----	-----	-----	47.0	32.5	7.0	6.0	7.0	0.5	35	38	16	10	1
35	-----	-----	-----	33.5	47.0	2.5	1.0	15.5	0.5	36	34	24	6	0
36	-----	-----	-----	37.5	49.0	4.0	3.0	6.5	0.0	28	46	19	6	1
37	-----	-----	-----	54.0	17.0	11.0	9.0	9.0	0.0	31	47	22	0	0
38	-----	-----	-----	52.5	8.5	10.0	2.0	26.5	0.5	27	37	30	6	0
39	-----	-----	-----	49.0	29.5	5.5	1.5	13.0	1.5	27	46	23	4	0
40	-----	-----	-----	54.0	15.5	18.5	4.0	6.5	1.5	16	37	35	12	0
41	-----	-----	-----	50.0	11.0	8.5	8.5	21.0	1.0	14	39	28	16	3
42	-----	-----	-----	24.5	27.0	5.5	2.0	38.5	2.5	34	46	20	0	0
43	-----	-----	-----	43.5	45.5	5.5	2.5	1.5	1.5	54	41	5	0	0
44	-----	-----	-----	50.0	32.0	5.0	1.0	11.5	0.5	40	47	13	0	0
45	-----	-----	-----	42.0	33.0	6.0	7.0	11.5	0.5	30	43	22	4	1
46	-----	-----	-----	48.5	34.0	4.0	1.0	12.5	0.0	8	33	37	19	3
47	-----	-----	-----	69.5	14.5	2.5	1.0	11.5	1.0	33	44	16	7	0
48	-----	-----	-----	63.5	22.5	4.5	2.0	6.5	1.0	38	39	22	1	0
49	-----	-----	-----	35.5	25.5	10.0	0.0	29.0	0.0	13	39	44	4	0
50	-----	-----	-----	39.5	37.0	5.5	0.0	17.5	0.5	21	39	33	4	3
Average	93	-----	9,248	52.2	29.9	4.6	2.0	10.6	0.7	27.5	38.3	25.8	7.5	0.9

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## THE SO-CALLED X-BODIES AS ARTEFACTS IN GLASS SLIDES.<sup>1</sup>

By WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.<sup>2</sup>

*(From the United States Army Board for the Study of Tropical Diseases as they  
Exist in the Philippine Islands.)*

Dr. Andrew Balfour<sup>(1)</sup> has announced the finding of the so-called X-bodies in the blood of a patient suffering from urticaria. These bodies were first reported by Horrocks and Howell<sup>(2)</sup> who found them in a case of tertian malaria, in several cases of undetermined fever, in the citrated blood from a rabbit and in the blood of oxen. They describe the X-bodies as follows:

"The bodies, when stained, were characterized by a faint capsule with a circular centre staining deep blue; they varied in size, some being as large as a red corpuscle, others only about one-eighth the size of a red corpuscle. In addition to these forms, which were the most common, the following were also seen: (a) A small blue circular centre surrounded by four or more faint capsules, concentrically arranged; (b) two circular bodies, each having a dark blue central point surrounded by a light blue ring, enveloped in one capsule which appeared indented as if two capsules were in the process of formation; (c) similar to (b) but the part surrounding the deep blue centre stained a deeper blue, and two indented capsules were seen; (d) a dark blue central part shaped like a crescent, containing a small circular body, with a deep blue central point within the arms of the crescent. None of the bodies on the slide showed any signs of chromatin."

Neither Horrocks and Howell nor Balfour commit themselves as to the nature of these bodies. Indeed, the former authors say, "Having in view the diverse nature of the cases in which the X-bodies were found, we are not justified in considering that they were the cause of the pathological conditions observed." It occurred to Balfour that such bodies might be contaminations from the skin, but this idea was subsequently dismissed, and none of these investigators appear to doubt that the bodies were really obtained from the blood. Fortunately they both furnish good and detailed drawings which permit of easy identification of the X-bodies.

<sup>1</sup> Published by permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> Weston P. Chamberlain, major, Medical Corps, United States Army and Edward B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

We believe that we can point out the nature of these bodies, and that we should do so, not only because two papers have been published on the subject, but because it has come to our knowledge that other investigators have been misled by them. Therefore, a statement of their true nature may simplify investigations in the future.

These peculiar bodies were first observed by one of us in 1907 while studying the blood of dengue, and before the publication of the paper by Horrocks and Howell. They were at first thought to be parasites associated with that disease, but further study showed that they were frequently present in normal blood. Subsequently they were found again in specimens from various pathologic conditions, and from different parts of the body, and the idea was finally suggested that they were artefacts in the glass slides. Search of a number of plain unstained glass slides having no specimens on them revealed the fact that these bodies could be found on many. On such unstained slides the bodies have the same morphology, but are without coloration. When the glass slide is previously stained with a little Wright's stain, as though staining a blood film, the bodies take on exactly the appearance described and accurately depicted by Horrocks and Howell and by Balfour.

The X-bodies in these two papers are, therefore, artefacts of some sort, present in certain of the glass slides for microscopic use. We think that they are found more often in old slides which have been used several times, and have been kept for some time in the Tropics. We believe that anyone finding the X-bodies in a preparation can readily verify our statement by staining and examining some of his slides on which no smear has been made. The bodies are not in the stain, because they may be found in unstained preparations.

Other facts that confirm these observations are: 1. The X-bodies have been found on slides made under a great diversity of conditions from both men and animals, including the blood from cases of malaria, undetermined fever, urticaria and dengue, and normal blood in the human, and also the blood of oxen and rabbits and the liver of oxen. We have observed them in slides containing scrapings of skin mounted in liquor potassæ. 2. In the same case the bodies are not found constantly, but are only seen in a few out of many smears, although they are usually numerous in the particular slides in which they are observed. If present in the circulating blood, they should be found on all or nearly all the slides examined from the case at the same time, though not necessarily in large numbers. 3. So far as we are aware the bodies have never been detected anywhere except in smears or preparations made on glass slides.

As further evidence in favor of the X-bodies being in the surface of the slide we performed the following experiment:

A blood smear was stained with Wright's stain and showed many brightly colored X-bodies of various sizes. Several large ones were located with the vernier scale of the mechanical stage. The slide was then removed and scrubbed with water and gauze. On again bringing the located areas under the lens no blood corpuscles could be seen but the X-bodies were still there and unchanged in appearance except that the coloration was less intense. The slide was again removed, scrubbed with alcohol, and replaced beneath the lens. The identical X-bodies were present in the same locations as before, but all trace of the stain had been removed from them.

If a clean new slide containing no specimen is stained in the usual manner with Wright's stain, and the stain-film is then rubbed off with dry gauze or with xylol, X-bodies, still showing coloration, may be found. This fact suggests that the objects named X-bodies in most instances may be due to minute portions of the stain being retained mechanically in microscopic pits in the glass. Usually, the X-bodies are seen to be at a lower level than the blood corpuscles on a slide. We rarely have found instances where they appeared to be above the corpuscles and the edge seemed to overlap a red cell. Such an appearance could hardly have been due to a pit, but might be caused by a minute scale of glass on the surface of the slide, which would entangle the stain and beneath which the edge of a corpuscle could slip. The slide on which this overlapping was noted is the one described in the preceding paragraph and the X-bodies which appeared to have the edges slightly overlying red cells were the ones which remained unchanged in location after repeated scrubbing.

Photomicrographs of these bodies are appended. The photographs were made by Mr. Charles Martin of the Bureau of Science, to whom we desire to express our obligation. The magnification in all cases is 1,000 diameters. The first three figures are photographs of X-bodies found on a slide containing a smear of normal human blood, while the last three are of bodies that were found on a glass slide containing no specimen of any kind, but which had been stained with Wright's stain and the dry stain-film then rubbed off with a piece of gauze. The bodies were very numerous on these slides, a number being present in nearly every field, but it is almost impossible to procure good photographs of more than one or two on a single negative owing to the difficulty of obtaining an accurate focus on several of them at the same time.

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## ILLUSTRATIONS.

---

### PLATE I.

FIGS. 1, 2, and 3. X-bodies on slides smeared with normal blood.  $\times 1,000$ .

FIGS. 4, 5, and 6. X-bodies on a clean slide which had been stained with Wright's stain and the stain-film rubbed off with gauze.  $\times 1,000$ .

Photomicrographs by Charles Martin of the Bureau of Science, Manila.



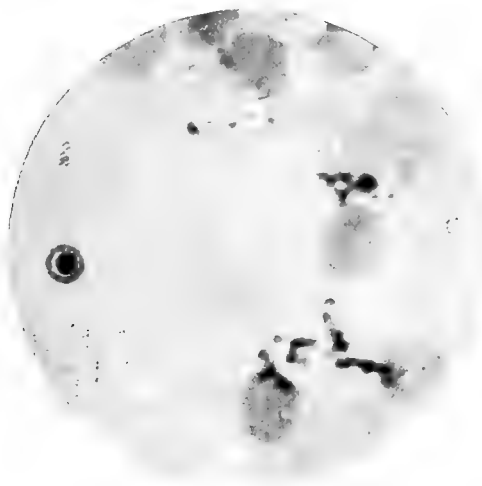


Fig. 1.

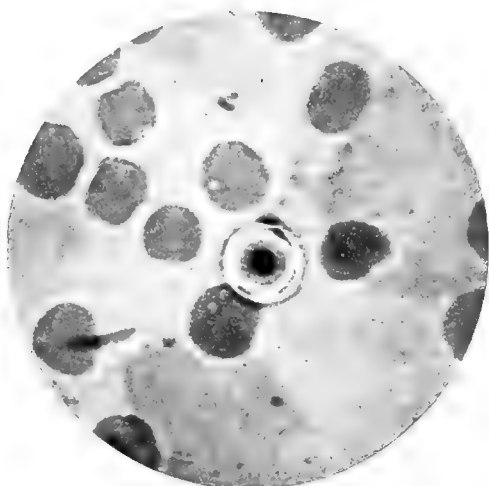


Fig. 2.

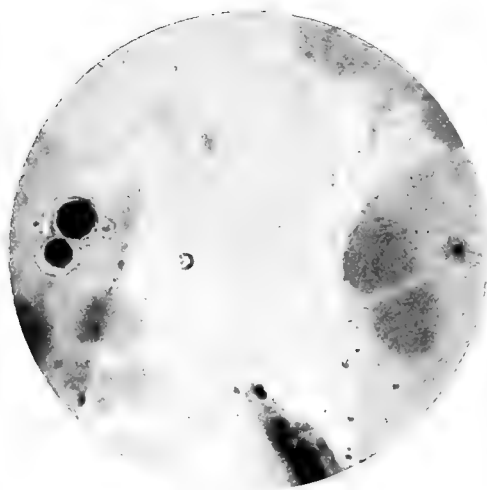


Fig. 3.

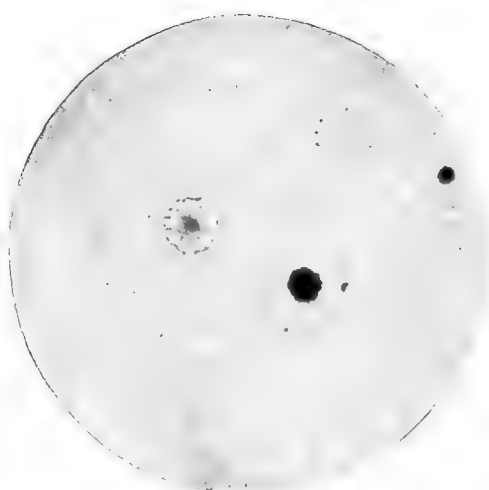


Fig. 4.

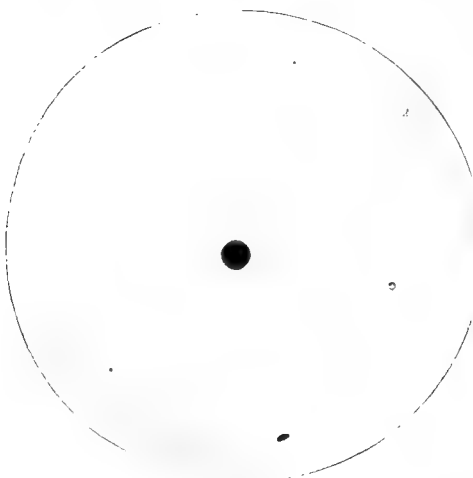


Fig. 5.

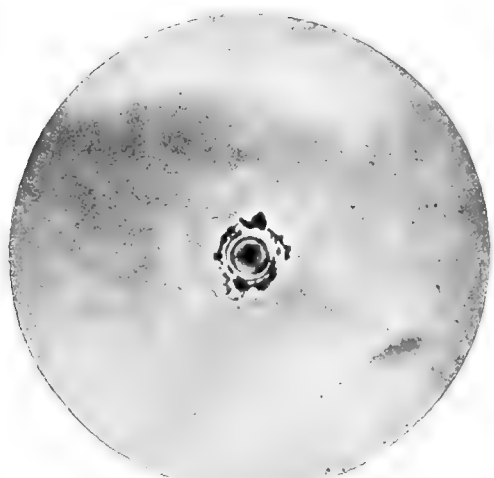


Fig 6.



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OSCAR TEAGUE, M. S., M. D.; W. E. MUSGRAVE, M. D.

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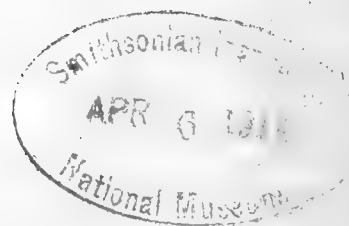
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## OBSERVATIONS ON THE INFLUENCE OF THE PHILIPPINE CLIMATE ON WHITE MEN OF THE BLOND AND OF THE BRUNETTE TYPE.<sup>1</sup>

---

BY WESTON P. CHAMBERLAIN.<sup>2</sup>

*(From United States Army Board for the Study of Tropical Diseases.)*

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- PART I. INTRODUCTION: SOURCES OF EVIDENCE: GEOGRAPHY AND CLIMATE: SUN-LIGHT.
- PART II. PHYSICAL EXAMINATIONS AND LABORATORY TESTS ON BLONDS AND BRUNETTES OF THE 1909-GROUP AND THE 1910-GROUP.
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- PART IV. SYMPTOMATOLOGY AND DIETARY HABITS FOR THE 1910-GROUP AND FOR THE SCOUT-CONSTABULARY-POLICE-GROUP.
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- PART VIII. DISCUSSION OF CLIMATIC INFLUENCES AND PIGMENTATION: GENERAL SUMMARY: CONCLUSIONS.

<sup>1</sup> Published with permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> Weston P. Chamberlain, major, Medical Corps, United States Army, president of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

PART I. INTRODUCTION ; SOURCES OF EVIDENCE ; GEOGRAPHY AND CLIMATE ;  
SUNLIGHT.

## INTRODUCTION.

The influence of a tropical climate on men, especially the members of the Caucasian race, is an extremely complex subject. Among the general factors to which, with greater or less weight of authority, the deleterious effects of tropical residence are alleged to be due may be mentioned heat, humidity, chemical action of the sunlight, lack of exercise, disturbed sleep, improper food, bad water, alcoholic and venereal excesses, and, perhaps most important of all, infections with those animal and vegetable pathogenic organisms which are confined more or less exclusively to hot regions. Individually age, sex, race, stature, previous residence, personal immunity, and perhaps complexion have to be given consideration.

The work herein reported has to do with only one of the above factors, namely the complexion type. The distribution of the black and brown races in the hotter portions of the globe and the difficulties which in the past attended the colonization of the Tropics by the Caucasian were matters of common observation long before the causes of tropical disease and deterioration received any adequate study. More recently several authors have claimed that the blonds tend to decrease in numbers or to deteriorate when they are transplanted from the relatively cloudy regions of northern Europe to sections in the Temperate Zone which have a much greater amount of sunshine. Woodruff, studying this phase of the subject in the Philippines, maintains that the blonds suffer more severely than do the brunettes from the deleterious influence of tropical residence and that the ill effects observed among white men dwelling in the Torrid Zone are due mainly to the large proportion of chemical or ultra-violet rays contained in the tropical sunlight. (2) (3)

To determine what may be the influence of the actinic rays alone, as distinguished from the other factors enumerated in the first paragraph, is evidently well-nigh impossible. The question as to whether transplanted fair-skinned races gradually change after many generations from a lighter to a darker average type, as a result of the survival of those best fitted to endure a high degree of sunlight, is purely speculative and of theoretical interest only. Whether men of dark complexion living ten, twenty, or thirty years in the Tropics can withstand the climatic influences more successfully than those having fair skin, light hair, and blue eyes is of much practical importance, but is extremely difficult to determine because of the almost insurmountable obstacles which stand in the way of making observations over such a period of time on any considerable group of men. When it comes to the relative resistance of the blonds and the brunettes during the comparatively short tour of duty (two years) which American soldiers commonly serve in the Phil-

ippines, the task is beset with fewer difficulties and it is to the elucidation of this problem that our efforts have been directed during the last thirty months. The matter is of some practical importance in the selecting of recruits and civil service employees for tropical countries.

#### SOURCES OF EVIDENCE.

The evidence on which this report is based is of several kinds and derived from various sources. It may be divided into classes as follows:

CLASS I. A series of observations carried out under the supervision of the Board, during the calendar year 1909, on enlisted men of the United States Army. This will be called the "1909-Group." One hundred and fifty-seven blonds and 154 brunettes were observed. Besides the symptomatology and the sick record over a period of two years for these men, there were made 1,100 weight, 1,320 pulse rate, 1,320 respiration rate, 1,320 temperature, 880 blood-pressure and 880 dynamometer observations, spaced at equal intervals throughout one year.<sup>3</sup> There were performed by the Board 195 red blood cell counts, 195 hæmoglobin estimations, 38 leucocyte counts, and 57 differential counts.

CLASS II. A series of observations carried out under the supervision of the Board during the calendar years 1910 and 1911 on enlisted men of the United States Army. This will be called the "1910-Group." Three hundred and forty-seven blonds and 346 brunettes were observed for one year. Besides recording the sick record,<sup>4</sup> symptoms, effects of tropical residence and sunlight, habits as to food and alcohol, characters, court-martial trials, fines and confinements, there were made on the men, 3,694 weight, 3,986 pulse rate, 3,986 respiration rate, 3,986 temperature, 2,540 blood-pressure and 620 dynamometer observations, 1,134 hæmoglobin estimations, 1,134 red blood cell counts, 1,152 urine and 601 stool examinations.<sup>5</sup> These observations were spaced at regular intervals throughout a year. There were performed by the Board 118 leucocyte estimations, 90 differential blood counts, and 56 Arneth counts on blond and brunette Americans, and, for comparison, 552 blood-pressure estimations on 386 Filipinos and 50 differential and Arneth counts on 50 Filipinos.

CLASS III. A collection of data from the commissioned officers of the Philippine Scouts and the Philippines Constabulary and from the Americans in the Manila police force. These are men who have been a long time in the Philippines, the average period of continuous tropical service being 5.5 years. There were 186 blonds, 147 brunettes, and 235 of a mixed type in this group. As a class they are men who do a large amount of work out of doors and exposed

<sup>3</sup> The observations referred to in this sentence were made under the supervision of the Board, by the following medical officers of the United States Army: Major C. C. Collins and Captains C. D. Cowles, jr., G. L. McKinney, and H. A. Phillips.

<sup>4</sup> The sick record covered a period of over twenty-two months.

<sup>5</sup> The observations referred to in this sentence were made under the supervision of the Board, by the following medical officers of the United States Army: Majors A. E. Truby and Roger Brooke, jr.; Captains E. G. Bingham, John R. Barber, Mahlon Ashford, E. G. Huber, H. M. Snyder, and W. L. Hart; First Lieutenants J. B. H. Waring, W. R. Dear, C. E. Doerr, F. S. Wright, C. G. Snow, N. L. McDiarmid, Armin Mueller, T. J. Leary, M. C. Stayer, L. C. Garcia, and C. E. Fronk, Medical Corps; and First Lieutenants W. F. de Niedman and C. A. Betts, Medical Reserve Corps.

to the sun. These individuals are considered in what we will term the "Scout-Constabulary-Police-Group."

CLASS IV. An examination of all patients invalidated home from the Division Hospital in Manila during a period of one and one-half years and a determination of the complexion type of each. There were 273 of these men.

CLASS V. An examination of 10,072 enlisted men of the United States Army to determine the relative proportions of the blond, brunette, and mixed types. The rate per 1,000 was found to be, blonds 238, brunettes 206, mixed types 556. This information was used as a basis for comparison with the rates per 1,000 of the three types in Classes III and IV, the former consisting of men who had voluntarily endured the climate for an average of 5.5 years and the latter of men who had succumbed to its influences during their tour of military service.

CLASS VI. A series of cases of sunstroke and heat exhaustion occurring in the United States and in which the type of complexion of the patient was recorded.<sup>6</sup>

In Class II, the choice of the blonds and brunettes for observation was made by the medical officers referred to in footnote 5, and the selected men were subsequently all examined by the writer, and those who did not conform to the standard types were excluded. In Class I, selection was made by choosing from the cards of a group of 800 men, who had been under observation for two years, those on which the 3 recorded complexion factors indicated well marked blondness or a clearly defined brunette type. Throughout this report the blond group includes men with blue or gray eyes, light brown, red, flaxen, or sandy hair, and fair, ruddy, or light complexion, while the brunette group is made up of those with brown or black eyes, dark brown or black hair, and medium or dark complexions. Men in whom one of the complexion factors corresponded to a certain type and the other two belonged to the opposite type were classed as "mixed," and were excluded from the observations dealt with in Part II.<sup>7</sup>

Each of the officers referred to in footnotes 3 and 5 had under ob-

<sup>6</sup> These statistics were collected through the kindness of the authorities at the following hospitals, to whom we wish to express our appreciation of the courtesies extended to us: Philadelphia General Hospital; Roosevelt Hospital, New York, Bellevue Hospital, New York; Massachusetts General Hospital, Boston; Presbyterian Hospital, New York; Boston City Hospital; Carney Hospital, Boston; St. Luke's Hospital, Chicago; Mercy Hospital, Baltimore; Jefferson Hospital, Philadelphia; New Haven Hospital; Alexian Brothers' Hospital, Chicago; Cook County Hospital, Chicago; St. Louis City Hospital; Rhode Island Hospital, Providence. We also received reports from a few other institutions, but as they came in our franked envelopes without address we are unable to credit them to the sender.

<sup>7</sup> With such a classification there will be a very well marked average difference in complexion type between the blond group and the brunette group. However, it must not be thought that all of the blonds were conspicuous examples of blondness. A man with dark blue eyes, light brown hair, and a fair skin would fall in the blond class and, while not a conspicuous blond, would still be sharply contrasted with the man of dark brown eyes, black hair, and swarthy complexion.

servation approximately equal numbers of the blonds and of the brunettes, and therefore in considering the final results the personal factors of the different observers need not be considered. The conditions under which the men of the blond and of the brunette type lived during the observation period were identical in all known respects.

#### GEOGRAPHY AND CLIMATE OF THE PHILIPPINES.

The observations were made at various localities in an Archipelago consisting of many hundreds of mountainous islands extending in latitude from  $21^{\circ}$  north to  $5^{\circ}$  north. No point even in the larger islands is in excess of 100 kilometers from the sea. With the exception of Camp Stotsenburg, John Hay, and Keithley, all of the military posts where the observations were conducted are located on or close to the coast-line and elevated but a few meters above the sea level.<sup>8</sup> Camp Stotsenburg is located about 50 kilometers from salt water on a plain at an altitude of about 200 meters. Its climate does not differ materially from that of the coast stations. Camp John Hay and Camp Keithley are in the mountains at altitudes of 1,500 and 800 meters respectively, and are characterized by a much lower temperature and a higher degree of cloudiness than are the lowland stations. The observations made at these two posts are not included in the general averages and were used merely for comparison with the lowland groups.

Although everywhere tropical yet the climate of the Philippines varies considerably in different localities as a result of altitude, influence of mountain ranges, and proximity to the sea. In the regions where most of the observations were carried out the hot and dry season is in April, May, and June. The rains come with the cessation of the northeast monsoon in June or July and persist till October or November. The differences in temperature between the warm season and the cool season are quite noticeable. In the posts in Mindanao and Jolo the differences of season, as regards both temperature and rain, are less clearly marked, and, as a result of several factors, the heat is no greater than on the northern coast of Luzon, over 1,200 kilometers more distant from the Equator, and indeed is less intense than in many of the central parts of the Archipelago.

Complete details as to the climate of the Archipelago can be obtained from Bulletin No. 2, Census of the Philippine Islands, entitled *The Climate of the Philippines*. A few figures are collected from this publication to show the more important climatological features at different points.

<sup>8</sup> Fort William McKinley and Camp Jossman are each about 7 kilometers inland, but are little elevated above the sea. Fort Mills is on an island about 2 kilometers wide, but its highest ridge, where the barracks are located, is 200 meters above sea level.

TABLE I.—*Annual thermic oscillation in the Philippine Archipelago.*<sup>a</sup>

Place.	Annual oscillation.		Latitude (north).		Place.	Annual oscillation.		Latitude (north).	
	°C.	°F.	De-grees.	Min-utes.		°C.	°F.	De-grees.	Min-utes.
Aparri-----	6.5	11.7	18	22	Iloilo-----	3.8	6.8	10	42
Tarlac-----	5.2	9.4	15	31	Ormoc-----	2.8	5.0	11	00
Arayat-----	4.6	8.3	15	8	Cebu-----	2.7	4.9	10	18
Manila-----	3.5	6.3	14	35	Davao-----	2.2	4.0	7	1

<sup>a</sup> This indicates the variation of the *mean* monthly temperature and not the *extreme*.

For Manila, which is representative of most of the region under consideration in this report, the normal monthly means of temperature for the period 1883-1902 are shown in Table II. The maximum recorded temperature in Manila (May, 1889) was 37° C. (100° F.), and the minimum (Jan, 1907) was 15° C. (59° F.).

TABLE II.—*Normal monthly means, Manila.*

Month.	°C.	°F.	Month.	°C.	°F.
January-----	25.0	77.0	July-----	27.1	80.7
February-----	25.4	77.7	August-----	27.1	80.7
March-----	26.8	80.2	September-----	27.0	80.6
April-----	28.3	82.9	October-----	26.9	80.4
May-----	28.6	83.4	November-----	26.1	79.0
June-----	27.9	82.2	December-----	25.2	77.3

The rainfall for the sections where the blond-brunette observations were being carried out ranges from 205 to 256 centimeters per year.<sup>9</sup> The degree of cloudiness is of much importance in an observation having to do with the possible influence of tropical light. The average cloudiness for Manila is given below, the scale being from 0 for a clear sky to 10 with the sky entirely covered. The table also shows the average of clear and variable days and the average hours of sunshine.

TABLE III.—*Average cloudiness, average clear and variable days, and average hours of sunshine monthly in Manila.*

Month.	Average cloud- iness.	Average clear and variable days.	Average hours of sunshine.	Month.	Average cloud- iness.	Average clear and variable days.	Average hours of sunshine.
January-----	4.6	23.9	193	August-----	7.5	14.0	143
February-----	3.8	23.8	220	September-----	7.4	13.1	135
March-----	3.8	23.9	247	October-----	6.1	17.1	172
April-----	3.5	25.1	264	November-----	5.8	18.6	160
May-----	5.1	19.9	220	December-----	5.6	22.6	157
June-----	6.8	17.3	160	Mean-----	5.6	19.5	184.8
July-----	7.5	14.9	147				

<sup>9</sup> This does not include Camp John Hay and Camp Keithley where the rainfall is much higher.

Comparing the average number of hours of sunshine with the figures for certain places in the United States it will be found that Manila receives 51 per cent of the theoretical sunshine while New York receives 56 per cent, Chicago 57 per cent, Denver 69 per cent, and Santa Fe 76 per cent.(1) In other words numerous regions in the temperate United States are characterized by many more hours of sunshine than are the tropical Philippines. These figures of course do not take into consideration the question of intensity of the sunlight in the two zones.

The quantity of watery vapor in the atmosphere has a direct influence on the climate, because it checks to some extent the radiation of heat, and the relative humidity is of still greater importance in studying the influence of climate on man because the greater the humidity the more marked is the interference with the thermolysis of the body resulting from the evaporation of perspiration.(21) The following table shows the monthly and annual averages in Manila for a period of twenty years. These figures may be compared with average relative humidity records for July of 70.6 per cent for Chicago, 70.4 per cent for New York, 71.0 per cent for Washington, and 72.3 per cent for New Orleans.

TABLE IV.—*Monthly and annual averages of relative humidity in Manila, per cent.*

Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Annual average.
77.6	74.2	71.8	70.7	76.7	81.4	84.8	84.8	85.5	82.7	82.0	80.7	79.4

In most parts of the Archipelago the discomfort one would expect from the continued high temperature and humidity is greatly mitigated by the very general presence of refreshing breezes, particularly at midday and in the afternoon and early evening. The velocity and frequency of the wind in the vicinity of Manila is greatest during the season when the temperature elevation is the greatest (March to September). The average daily velocity of the wind for Manila is 217.8 kilometers, the monthly averages varying from 149.3 in December to 291.0 in September.

#### ACTINIC POWER OF THE SUNLIGHT.

Of late years the chemical activity of the sunlight has become a factor which, in the opinion of many, should be considered in discussing climate and its influences. Freer,(1) Gibbs,(14) and Bacon,(15) at the Bureau of Science in Manila, have found that the tropical sunshine produces chemical changes which take place either more slowly or not at all in temperate climates. It has also been shown by Freer that there are in the Philippines "actinic" and "nonactinic days," the chemical action of the sunlight during the latter being much less powerful, even though the sky may seem as clear as on an actinic day. The causes of these differences have not been determined. The investigations at the Bureau of Science have shown that the spectrum of the sun's rays extends into the ultra-violet little if any farther in Manila than in temperate regions.(4)

That concentrated ultra-violet rays have a harmful influence on bacteria, as well as on some higher forms of life such as protozoa, has been clearly proven by many observations made by ourselves(18) and by others.(19) Some writers, notably Woodruff,(2)(3) have considered that such rays were very injurious to white men, more especially to

those of the blond type. The subject needs much more study before a definite conclusion can be reached regarding the influence of the chemical rays of the solar spectrum, but the recent work by Aron<sup>(4)</sup> seems to indicate that the deleterious influence of the tropical sunlight on men and animals is due to the long heat-rays rather than to the short length ultra-violet waves. Steinmetz<sup>(5)</sup> considers ultra-violet radiations of moderate intensity, such as occur in sunlight, to be harmless to the eyes. When acting on the skin ultra-violet rays have little power of penetration, being absorbed by the blood, but whether they can produce such changes in that fluid as to lead to constitutional disturbances still remains an unsettled problem.

PART II. PHYSICAL EXAMINATIONS AND LABORATORY TESTS ON BLONDS AND BRUNETTES OF THE 1909-GROUP AND THE 1910-GROUP.

The work on the 1909-Group began in the first quarter of 1909 and ended in December of that year, there being records for each man of 4 observations evenly spaced over an interval of about eleven months. The examinations of the 1910-Group began in the second quarter of the year 1910 and ended at the same time in 1911, there being for each soldier 5 complete observations spaced at approximately three-month-intervals during the period of one year. The observations were made under our supervision by the gentlemen named in footnotes 3 and 5. All of these officers are thoroughly familiar with the laboratory methods involved in the work, and the number of observers minimizes the influence of the personal equation.

It should be understood that the men under observation were healthy soldiers, any who showed evidence of disease having been excluded before the beginning of the observation period. The length of time the men had served continuously in the Philippines at the commencement of the test varied from two months to several years.<sup>10</sup> The average length of the present tour of tropical service at the beginning of the year of observation was in the 1909-Group for the blonds 14.9 months and for the brunettes the same. In the 1910-Group it was for the blonds 6.4 and for the brunettes 6.7 months. In both groups it will be seen that the average period of tropical service prior to the commencement of the observations was sufficient for the preliminary stimulating effect of the Tropics to have passed away. At the beginning of the observation period the total tropical service, including present and previous tours, in the 1910-Group was 32.9 months for the blonds and 34.4 months for the brunettes. In the 1909-Group the average height was the same for both blonds and brunettes, 67.4 inches (171.1 centimeters), and the average age was practically the same, 25.5 years for the blonds and 25.1 for the brunettes. In the 1910-Group the average height was 67.8 inches (172.2 centimeters) for the blonds and 67.3 inches (170.9 centimeters) for the brunettes, and the average age was 27.4 years for the blonds and 28.1 years for the brunettes.

<sup>10</sup> The men with several years' service had voluntarily transferred from organizations going home to others just arriving in the Islands. One man we have in mind was a most conspicuous blond and had been twelve years continuously in the Philippines, remaining in perfect health.



These soldiers were dressed in a loose fitting uniform made of khaki-colored drilling and habitually wore white cotton undershirts and drawers. The headgear for nearly all consisted of a narrow-brimmed helmet covered with khaki cloth. In general the clothing was the same for the men of the Scout-Constabulary-Police-Group which is to be considered further on.

The observations on both the 1909-Group and the 1910-Group will be taken up together and discussed under various subheads.

*Weight.*—The maintenance of a weight proportionate to the height is generally considered one of the best guides to the health of the individual and, therefore, the average of the individual weight observations was deemed of much importance in deciding whether a difference was manifest between the blond and the brunette groups. The results are shown in the following tables.

TABLE V.—Comparative average weights of 111 blonds and 118 brunettes, 1909-Group.

Type.	Height.		Weight.									
			First quarter.		Second quarter.		Third quarter.		Fourth quarter.		Loss for year.	
			Lbs.	Kgms.	Lbs.	Kgms.	Lbs.	Kgms.	Lbs.	Kgms.	Lbs.	Kgms.
Blond	67.4	171.1	142.8	64.9	141.4	64.3	140.7	64.0	140.2	63.7	2.6	1.18
Brunette	67.4	171.1	144.5	65.6	142.7	64.9	142.7	64.9	141.8	64.5	2.7	1.23

TABLE VI.—Comparative average weights of 307 blonds and 301 brunettes, 1910-Group.

Type.	Height.		Weight.											
			Second quarter 1910.		Third quarter 1910.		Fourth quarter 1910.		First quarter 1911.		Second quarter 1911.		Loss for year.	
			Lbs.	Kgms	Lbs.	Kgms	Lbs.	Kgms	Lbs.	Kgms	Lbs.	Kgms	Lbs.	Kgms.
Blond ---	Ins.	Cm.	148.1	67.3	147.8	67.2	147.8	67.2	147.2	66.9	146.1	66.4	2.0	.91
Brunette	67.8	172.2	148.3	67.4	147.7	67.1	147.3	67.0	147.3	67.0	146.5	66.6	1.8	.82

On examining Tables V and VI it will be seen that both groups declined slightly and progressively in weight during the year of observation and that there was no significant difference in the degree of loss for the blond type and the brunette type. In the 1910-Group the blonds lost 0.2 of a pound (0.09 kilogram) more than the brunettes, but in the 1909-Group the conditions were reversed and the brunettes lost 0.1 of a pound (0.05 kilogram) more than the blonds. In either instance the differences in the respective losses of the two types are so trivial as to be of no importance.

*Temperature.*—The temperature observations were taken by mouth and in nearly all instances in the 1910-Group the thermometers were kept in for five minutes to insure registry of slight degrees of fever if present. The results appear in Tables VII and VIII.

TABLE VII.—*Comparative average temperatures of 111 blonds and 118 brunettes, 1909-Group.*

Type.	First quarter.		Second quarter.		Third quarter.		Fourth quarter.		Average for year.	
	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.
Blond -----	98.8	37.1	98.8	37.1	99.1	37.3	98.7	37.0	98.9	37.2
Brunette -----	98.9	37.2	98.8	37.1	99.0	37.2	98.6	37.0	98.8	37.1

TABLE VIII.—*Comparative average temperatures of 307 blonds and 301 brunettes, 1910-Group.*

Type.	Second quarter 1910.		Third quarter 1910.		Fourth quarter 1910.		First quarter 1911.		Second quarter 1911.		Average for year.	
	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.
Blond ---	98.8	37.1	98.8	37.1	98.7	37.0	98.6	37.0	98.7	37.0	98.7	37.0
Brunette--	98.7	37.0	98.8	37.1	98.8	37.1	98.6	37.0	98.7	37.0	98.7	37.0

At one or more of the quarterly periods there were found among the men of both types some cases of elevation of temperature without assignable cause, but it will be obvious on examining the tables that these occurrences were not sufficiently numerous to raise the average temperature for the year materially above the recognized normal for temperate climates. The average temperature for the blonds at no quarterly period varied more than 0°.1 F. (0°.06 C.) from the corresponding figure for the brunettes, sometimes one type and sometimes the other showing the higher figure. For the whole year the average for the two types was the same for the 1910-Group and but 0°.1 F. (0°.06 C.) different in the 1909-Group. Therefore, it was concluded that as regards the maintenance of bodily temperature in the Tropics there were no constant differences between the blond and the brunette types.

*Pulse and respiration.*—The pulse and respiration were taken as a rule with the men seated. At the few posts where the record was made with the men standing the numbers of blonds and brunettes were approximately equal so the relative influence of this factor is the same for the two complexion types. The results are shown in Tables IX and X.

TABLE IX.—*Comparative average pulse and respiration rates of 111 blonds and 118 brunettes, 1909-Group.*

Type.	First quarter.		Second quarter.		Third quarter.		Fourth quarter.		Average for year.	
	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.
Blond -----	82.1	19.7	92.6	20.8	89.3	19.8	84.6	19.2	87.2	19.9
Brunette -----	83.1	20.6	91.5	20.7	93.5	20.7	85.6	19.2	89.2	20.3

TABLE X.—*Comparative average pulse and respiration rates of 307 blonds and 301 brunettes, 1910-Group.*

Type.	Second quarter 1910.		Third quarter 1910.		Fourth quarter 1910.		First quarter 1911.		Second quarter 1911.		Average for year.	
	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.	Pulse.	Respiration.
Blond ----	77.0	19.3	77.8	19.2	77.5	19.1	77.1	19.1	77.0	19.0	77.3	19.1
Brunette --	77.6	19.4	76.7	19.4	77.6	19.2	77.3	19.5	77.2	19.4	77.3	19.4

It is shown by the tables that the average pulse rate for the year is the same for both complexion types in the 1910-Group. In the 1909-Group it is two beats nearer the normal Temperate Zone standard for the blonds than it is for the brunettes. The quarterly variations are inconsiderable and variable, first one complexion type and then the other being the higher. For both types the rate is considerably above the accepted normal average for cool countries, the higher rate for the 1909-Group being, in our opinion, due to the fact that most of these observations were made immediately after the men returned from drill or a practice march. The respiratory rates on the average are a few tenths of a respiration lower for the blonds than for the brunettes, but for both types and at all quarterly observations are considerably higher than the accepted normal of 14 to 18 per minute for healthy adults in Europe and America. As would be expected an increase in the frequency of the pulse and the respiration go hand in hand and the increase of both rates in the Tropics is in accord with the observations of Jousset, Plehn, and others, but differs from the experience of Rattray.<sup>(7)</sup> The conclusion was reached that the brunettes show no advantage over the blonds as regards either pulse or respiration rates.

*Systolic blood-pressure.*—Nearly all the observations were made with the soldiers in the sitting posture. At a few posts the readings were taken when the men were reclining, but as this was done with equal frequency among the blonds and among the brunettes it does not affect the comparison for the two types, even if it were generally accepted, (which is not the case) that there is a material difference in the pressure as a result of these changes in position.<sup>(6)</sup> The instrument used was Cook's modification of the Riva-Rocci apparatus, with an 8-centimeter cuff. By a careful comparison of the same instrument on several hundred men, using both an 8-centimeter and a 12.5-centimeter armlet, it was found that the average reading with the latter was 8 millimeters lower than with the former. Therefore, in the tables the averages have been reduced to the basis of a 12.5-centimeter cuff by deducting 8 millimeters from the actual findings.

TABLE XI.—*Comparative average systolic blood-pressure with 12.5-centimeter armlet for 111 blonds and 118 brunettes, 1909-Group.*

Type.	Average age.	First quarter.	Second quarter.	Third quarter.	Fourth quarter.	Average for year.
	Years.	mm.	mm.	mm.	mm.	mm.
Blond .....	25.5	115.8	112.5	114.2	116.8	114.8
Brunette .....	25.1	118.6	115.3	115.1	118.2	116.8

TABLE XII.—*Comparative average systolic blood-pressure with 12.5-centimeter armlet for 206 blonds and 198 brunettes, 1910-Group.*

Type.	Average age.	Second quarter 1910.	Third quarter 1910.	Fourth quarter 1910.	First quarter 1911.	Second quarter 1911.	Average for year.
	Years.	mm.	mm.	mm.	mm.	mm.	mm.
Blond .....	27.4	116.3	118.5	117.7	117.4	118.0	117.6
Brunette .....	28.1	117.9	117.2	117.8	117.7	117.3	117.6

Since the blood-pressure is in reality an index of the functional capacity of the heart, as correlated with the peripheral and visceral resistance and the volume of the circulating fluid, it would seem that its determination should be an excellent indication of the circulatory condition of a group of men. It will be observed that the pressures recorded in the tables are in close accord with the findings of other tropical observers.<sup>(8)</sup> We have found the blood-pressure for Filipinos to be approximately the same as the figures given in Tables XI and XII. This feature together with other points relating to the blood tension in the Tropics will be discussed at length in a subsequent communication devoted to blood-pressure alone.<sup>(20)</sup> It will be sufficient at this time to point out that the average pressures throughout the year for the blonds and the brunettes of the 1910-Group were identical while in the smaller 1909-Group the difference was only 2 millimeters of mercury. If the two groups are combined we obtain an average for 317 blonds of 116.7 millimeters and for 316 brunettes of 117.3 millimeters. This is a difference of only 0.6 millimeter, an amount which is entirely without significance. It should be noted that the average ages of the two groups were approximately the same, the maximum difference being only 0.7 year.

*Dynamometer observations.*—These strength tests were made with the usual hand dynamometer which registers simply the force of the maximum grip. The results appear in Tables XIII and XIV.

TABLE XIII.—Comparative average dynamometer tests on 111 blonds and 118 brunettes, 1909-Group. Registered in kilograms.

Type.	First quarter.	Second quarter.	Third quarter.	Fourth quarter.	Average for year.	Gain for year.	Average height.	Average weight.
							cm.	Kilos.
Blond -----	51.7	52.1	51.1	53.0	52.1	1.3	171.1	64.1
Brunette -----	52.8	52.5	51.3	53.3	52.5	0.5	171.1	65.0

TABLE XIV.—Comparative average dynamometer tests on 31 blonds and 31 brunettes, 1910-Group. Registered in kilograms.

Type.	Hand.	Second quarter 1910.	Third quarter 1910.	Fourth quarter 1910.	First quarter 1911.	Second quarter 1911.	Average for year.	Gain for year.	Average height.	Average weight.
									cm.	Kilos.
Blond -----	Right---	54.0	52.5	53.2	54.5	54.2	53.7	0.2	173.0	67.0
Brunette ----	Right---	52.2	52.7	55.1	55.3	54.8	54.0	2.6	171.2	67.0
Blond -----	Left ----	49.2	48.0	48.9	50.3	50.0	49.3	0.8	173.0	67.0
Brunette ----	Left ----	47.6	48.2	50.2	50.3	50.8	49.4	3.2	171.2	67.0

The fact that the average strength of the grip increased during the year we believe to be due not to any definite increase in strength on the part of the groups, but rather to the acquisition, through practice and familiarity with the instrument, of an increased dexterity in compressing the dynamometer. In the large 1909-Group this gain was a little more marked for the blonds than for the brunettes. In the 1910-Group the gain in strength of grip in each hand was much more marked for the brunettes, but this group is so small (only 31 men of each type) that the element of chance assumes considerable importance. If all the right hand readings of the first and last observations for both the 1909-Group and the 1910-Group are averaged the gain in grip strength for the blonds is 1 kilogram and for the brunettes 0.9 kilogram, a trivial advantage in favor of the blonds. It will be noted that throughout both years the grip record of the blonds is generally a trifle less than that of the brunettes, but this is probably due to the slight advantage in physical development which the brunettes in the two groups seem to show, as evidenced by the relationship of their average weight and height as compared with the same data for the blonds.

On the whole it appears that the dynamometer tests failed to indicate that the brunettes possessed any appreciable advantage over the blonds as regards the maintenance of their strength.

*Hæmoglobin estimations and counts of the red blood cells.*—Most of the hæmoglobin estimations were made with the Dare hæmoglobino-meter and the blood counts were performed with the Thoma-Zeiss hæmocytometer. The results are given in the following tables:

TABLE XV.—*Comparative average hæmoglobin and red blood cell estimations on 26 blonds and 39 brunettes, 1909-Group.*

Type.	January.			July.			December.		
	Hæmo-globin.	Red cells.	Color index.	Hæmo-globin.	Red cells.	Color index.	Hæmo-globin.	Red cells.	Color index.
	<i>Per ct.</i>			<i>Per ct.</i>			<i>Per ct.</i>		
Blond.....	88.4	5,307,000	0.83	87.5	5,411,000	0.80	88.9	5,096,000	0.88
Brunette.....	89.8	5,255,000	0.85	88.7	5,317,000	0.83	90.7	5,189,000	0.87

TABLE XVI.—*Comparative average hæmoglobin and red cell estimations on 288 blonds and 279 brunettes at beginning and at end of observation period, 1910-Group.*

Type.	Second quarter 1910.			Second quarter 1911.		
	Hæmo-globin.	Red cells.	Color index.	Hæmo-globin.	Red cells.	Color index.
	<i>Per ct.</i>			<i>Per ct.</i>		
Blond.....	90.0	5,158,000	0.87	89.3	5,185,000	0.87
Brunette.....	90.5	5,063,000	0.89	89.9	5,229,000	0.86

In both groups we have obtained results similar to those previously reported by Wickline<sup>(9)</sup> and by Phalen of this Board<sup>(10)</sup>; namely, a red corpuscle count ranging above 5,000,000 and a hæmoglobin average approximating 90 per cent. Therefore the color index is low, our figures for different periods ranging from 0.80 to 0.89. Since the observations of about a dozen careful workers, comprising over 1,700 red cell counts and an equal number of hæmoglobin estimations, have all shown the same tendency, it appears to us certain that a high red corpuscle count and a rather low color index must be characteristic for the American who has lived one or two years in the Philippines.

When the two complexion types are compared it will be noted that in both the 1909-Group and the 1910-Group the differences, for corpuscular counts, for hæmoglobin and for color index, were slight and also were inconstant, at some observation periods the blonds and at others the brunettes being in the lead. If we combine and average the color indices for all the observations in each of the two groups it will be seen that the differences are only 0.014 for the 1909-Group and 0.005 for the much larger 1910-Group. Such slight variation are entirely without significance.

*Leucocyte estimations, differential counts, and Arneth counts.*—The white cell estimations were made with the Thoma-Zeiss blood counting instrument, and the differential and Arneth counts after staining films with Wright's stain. The examinations were made only at the end of the observation period of one year, a time when the men had served on the average for about twenty months continuously in the Tropics and in no individual case for less than fourteen months.

TABLE XVII.—*Comparative average leucocyte estimations and differential and Arneth counts for blonds and brunettes.*<sup>a</sup>

Type.	White count, per cu. mm.	Differential leucocyte count.					Arneth count.					Arneth index.
		Poly-nuc.	Small lymph	Large lymph	Eosin.	Baso-phile.	Class I.	Class II.	Class III.	Class IV.	Class V.	
		Per ct.	Per ct.	Per ct.	Per ct.	Per ct.						
Blond ----	6,980	54.8	34.3	6.2	3.9	0.9	11.5	31.6	38.2	16.2	2.1	43.1
Brunette --	7,155	59.6	29.9	6.0	3.8	0.8	14.5	34.5	35.7	13.6	1.8	49.0

<sup>a</sup> These observations were made mostly on the 1910-Group, but some were on the members of the 1909-Group. The leucocyte counts are the average for 89 blonds and 86 brunettes; the differential counts are the average for 45 blonds and 45 brunettes; the Arneth counts are the average for 28 blonds and 28 brunettes, these being a part of the 45 men on whom the differential counts were made.

That the polymorphonuclear neutrophile count is very low (ranging from 50 to 60 per cent) for Filipinos and for white men with a year or more of Philippine service has been shown by Wickline,<sup>(9)</sup> Guerrero and Sevilla,<sup>(11)</sup> and by several members of this Board.<sup>(10) (12)</sup> Recently Chamberlain and Vedder<sup>(13)</sup> have confirmed the earlier observations and have shown that there is a marked shift to the left in the Arneth count for healthy Filipino laborers and a slight tendency in the same direction for white men residing in the Archipelago. It appears possible that the low count for the polymorphonuclear cells (phagocytes), together with the shift to the left in the Arneth picture (in other words a higher Arneth index), may indicate diminished phagocytic power for the blood in question and a lowered resistance to such infections as are combated in whole or in part by phagocytosis. Applying this theory to the blonds and brunettes it will seem that the evidence from the two methods of counting is conflicting. The percentage of polymorphonuclear neutrophiles is lower for the blonds than for the brunettes,<sup>11</sup> but on the other hand the shift to the left in the Arneth picture is more marked for the brunettes than for the blonds. The difference between the average white cell counts per cubic millimeter for the two types is so slight as to be unimportant.

<sup>11</sup> Wickline, examining soldiers with eighteen months of Philippine service, found the polymorphonuclear cells to constitute 54.3 per cent of the total leucocytes for blonds and 53.1 per cent for brunettes.<sup>(9)</sup>

From the foregoing it is concluded that the differential and the Arneth counts of this small series of men throw no light on the question of the relative resistance of the two complexion types.

*Urinary examinations.*—An examination of the urine was made on all of the men of the 1910-Group, once near the beginning and once near the end of the observation period, with a view to detecting any cases of nephritis. At the final examination albumin was found in 3 and casts in 3 of the brunettes while none of the blonds showed albuminuria and only 2 had casts. We attach no significance to these differences because of the small number of cases. An examination of the specific gravity averages are of some interest. The specific gravity of a single specimen of urine is of course in itself of little value, but when the specific gravity readings of single specimens from several hundred men are averaged the results have considerable importance in the direction of showing the condition of the group as regards renal elimination. It has been urged by some that in the Tropics there is a tendency to renal insufficiency, while others have considered that, as a result of excessive loss of fluid in the form of perspiration, the urine becomes too concentrated and is therefore irritating. The following table shows that the average specific gravity readings for the blonds and for the brunettes showed no differences worthy of consideration, and also that for both types the figures were those that are considered normal in the temperate zone. This latter opinion is based on 1,152 readings on 576 individuals which gives an average specific gravity of 1,019.8. The average 24-hour amount of urine is not known.

TABLE XVIII.—*Comparative average specific gravity readings for urine of 294 blonds and 282 brunettes, comprising 1,152 separate examinations, 1910-Group.*

Type.	Second quarter.	
	1910	1911
Blond .....	1,019.6	1,019.5
Brunette .....	1,020.2	1,019.8

*Stool examinations.*—At the completion of the year of observation, examinations were made of the stools of 308 blonds and 293 brunettes of the 1910-Group in order to determine if the two types showed any differences in the degree of infestation with intestinal parasites, especially uncinaria. No special search was made for amœbæ and no cathartic was given before obtaining the specimens. Three cover glass preparations were examined for each individual. The results are shown below.



TABLE XIX.—Comparative numbers of men infested with intestinal parasites among 308 blonds and 293 brunettes, 1910-Group.

Type.	Uncinaria.	Ascaris.	Trichocephalus.	Strongyloides.	Tænia.	Strongylus subtilis.	Balantidium.	Amœba coli.	Amœba dysenteriae.	Hymenolypis.	Cercomonas.
Blond-----	7	13	8	2	0	1	1	1	0	0	9
Brunette----	7	8	9	2	1	1	0	6	5	2	4

This table does not indicate as high a rate of infestation for blonds as for brunettes except with ascaris and cercomonas, which have little if any significance. The rate of hookworm infestation was slightly greater for the brunettes. This work confirms the previous observations of the writer<sup>(16)</sup> as to the infrequent occurrence of uncinariasis among American soldiers serving in the Philippines.

*Special observations after exercise.*—These examinations were made on the 1910-Group, once near the beginning and once near the end of the year of observation, with a view to determining whether the blonds became more easily exhausted by physical exertion than did the brunettes. The exercise preceding the examination was usually a practice march or a period of drilling, and was as nearly as possible the same for the two complexion types. The results are tabulated in the following table. For each kind of observation the time was the second quarter of the year, the first being in 1910 and the second in 1911.

TABLE XX.—Comparative average observations after exercise on 241 blonds and 292 brunettes, 1910-Group. Blood-pressures with 12.5-centimeter armlet.<sup>a</sup>

Type.	Weight.		Pulse.		Respiration.		Temperature.		Blood-pressure.	
	1910	1911	1910	1911	1910	1911	1910	1911	1910	1911
	Kgms.	Kgms.					°C.	°C.	mm.	mm.
Blond -----	66.6	66.4	85.9	82.7	21.2	20.8	37.2	37.0	125.4	123.8
Brunette ----	65.9	65.9	87.4	83.8	21.8	21.0	37.2	37.1	128.2	125.7

<sup>a</sup> The weights are the average for 169 blonds and 158 brunettes and the blood-pressures for 136 blonds and 124 brunettes.

On comparing this table with the preceding ones, which show the same class of observations when the men had not exercised, it is seen that as a result of the exertion there was a small average loss in weight, approximately 1 pound (0.5 kilogram), and a slight average increase in respiration rate and temperature, the increase of the former approximating two inspirations per minute and the latter 0° 1 C. The pulse rate was accelerated considerably, ranging from 5 to 10 beats per minute in excess of the rate when the men were at rest, and the systolic blood-pressure

was elevated more than 8 millimeters of mercury above the resting average. These are the effects which one would expect from moderate exercise indulged in by healthy, well trained men in hot weather. When we come to compare the two complexion types, it is interesting to note that the effects of the exertion were slightly more marked on the brunettes than on the blonds in all but one of the 20 observation averages, and in that one they were equal. The figures for examinations after exercise, as contrasted with those when the men were at rest, show that the loss of weight was a little more pronounced, and the elevation of the pulse, temperature, respiration, and blood-pressure was slightly more marked for the brunettes than it was for the blonds. We would not for a moment argue, because of these slight differences, that the brunettes are less fit than the blonds, but the figures certainly strongly indicate that the brunettes are *no better* able to endure exercise in the Philippines than are their fair skinned comrades.

#### SUMMARY OF PART II.

The differences between these exact observations on the blonds and on the brunettes are so slight and inconstant as to be of no significance. The tests fail to show any anatomical or physiological distinctions for the two complexion types in large groups of men who, at the end of the year of observation, had been continuously exposed to the Philippine climate for an average of 26.9 months in the case of the 1909-Group and 18.4 months in the case of the 1910-Group. This conclusion agrees with that reached by Wickline when examining American soldiers in the Philippines.<sup>(9)</sup>

#### PART III. RELATIVE AMOUNTS OF SICKNESS AMONG BLONDS AND BRUNETTES OF THE 1909-GROUP, THE 1910-GROUP, AND THE SCOUT-CONSTABULARY-POLICE-GROUP.

The relative number of admissions and of days on sick report for the blond and the brunette types in the 1909-Group and the 1910-Group is deemed to be of much value in this study, first, because of the large number of men considered (504 blonds and 500 brunettes) and, secondly, because of the long average period of tropical service over which the collection of the sick data extends. The statistics of sickness for the men have been obtained from their official sick record not only for the period of one year, during which the observations described in Part II were under way, but also for all the available continuous Philippine service of each man before the physical tests began and after they were concluded. As a result the sick records in the 1909-Group extend over an average period of considerably more than twenty-four months of unbroken tropical service. In the 1910-Group the average continuous Philippine residence during which the sick rates have been gathered is 22.4 months. For the combined groups the average approximates two years. The results are shown in Table XXI.

TABLE XXI.—Comparative numbers of admissions to sick report and days lost from sickness for 504 blonds and 500 brunettes of the 1909-Group and the 1910-Group.

Diagnoses.	Blonds.		Brunettes.	
	Admis- sions.	Days sick.	Admis- sions.	Days sick.
Diarrhœa and dysentery	74	822	68	569
Dyspepsia, indigestion, and gastritis	34	139	27	119
Constipation	18	63	28	82
Intestinal parasites	16	117	10	127
Coryza and bronchitis	25	178	12	56
Tonsillitis, pharyngitis, and catarrh	18	189	12	186
Malarial and undetermined fevers	95	638	93	586
Dengue fever	50	325	45	320
Neuralgia, myalgia and herpes zoster	9	66	12	150
Rheumatism; articular, acute, and chronic	5	58	11	291
Tuberculosis	5	69	3	75
Ringworm	18	178	17	136
Pemphigus, eczema, dermatitis, and ulcers	25	174	13	102
Furunculosis, carbuncle, cellulitis, and abscess	57	480	54	353
Lymphadenitis, nonvenereal	15	271	12	249
Appendicitis	4	83	4	54
Heat exhaustion	8	43	4	15
Diseases of eye and ear	16	368	14	276
Neurasthenia	2	52	1	19
Minor surgical conditions	41	616	41	519
Miscellaneous diseases	42	459	27	342
Accidental	129	1,375	121	1,202
Alcoholism and sequelæ	18	62	6	31
Venereal diseases	227	5,327	214	5,297
Total	951	12,152	849	11,156

Since the total numbers of men in each of the two complexion types are so nearly equal (504 and 500 respectively), we have not reduced the actual admissions and the actual days on sick report for each type to rates per 1,000, because such a reduction would not appreciably effect the comparison. It will be observed that the total number of admissions is 102 and the total number of days lost from sickness 996 greater for the blonds than for the brunettes. This means about 10 per cent more illness for the blond group. An advantage in favor of the brunettes is manifest for all of the more important causes of admission. While it must be admitted that there was considerably more sickness among the blonds under observation than among the brunettes, yet when it comes to a question of the occurrence throughout the whole Archipelago of the serious diseases which lead to invaliding home it will be seen that the brunettes were at a disadvantage as is to be shown further on in Table XXV.

*The Scout-Constabulary-Police-Group.*—For the sake of brevity this group will hereafter be referred to as the S-C-P-Group. It consisted of 568 men, of whom 186 were blonds, 147 brunettes, and 235 mixed types.

The reports from these persons cover an average of 5.5 years of continuous tropical service, the duration of Philippine residence for the individuals ranging from two to thirteen years. In reply to our questions as to illness a considerable proportion merely stated the number of times they have been sick and the cause of the disability, without giving the duration of the disease. Therefore Table XXII, which contains the data collected, simply shows the number of attacks of each illness, but does not give the days lost from sickness.

TABLE XXII.—*Comparative numbers of attacks of illness for the blonds, brunettes, and mixed types of the S-C-P-Group, while in the Philippines.*

Diagnoses.	Attacks of illness.					
	186 blonds.		147 brunettes.		235 mixed types.	
	Number.	Rate per 1,000.	Number.	Rate per 1,000.	Number.	Rate per 1,000.
Dysentery and diarrhoea .....	26	140	22	150	46	196
Malaria .....	58	312	60	408	68	289
Dengue .....	25	134	17	116	22	94
Fever, undetermined type .....	8	43	8	55	12	51
Appendicitis .....	8	43	10	68	10	43
Cholera .....	3	16	1	7	5	21
Pneumonia .....	6	32	0	0	1	4
Rheumatism .....	2	11	7	48	7	30
Indigestion .....	5	27	3	20	9	38
Typhoid fever .....	3	16	5	34	6	26
Neurasthenia .....	1	5	0	0	1	4
Skin diseases .....	3	16	0	0	4	17
Furunculosis .....	1	5	2	14	4	17
Ptomaine poisoning .....	3	16	3	20	4	17
Eye diseases .....	0	0	0	0	2	9
Accidental .....	3	16	7	48	4	17
Miscellaneous .....	13	70	18	122	48	204
Total attacks of illness .....	168	902	163	1,110	253	1,077
Never sick .....	85	456	53	361	90	383

For convenience in comparing, the admissions to sick report have been reduced to rates per 1,000 men of each type. First of all it is to be noted that the proportion of those *who had never been sick* is much higher for the blonds than it is for the brunettes. The total number of admissions for all diseases was considerably higher for the brunettes than for the blonds, 1,110 as compared with 902 *per mille*. Taking up the individual diseases it will be seen that the brunettes had a higher admission rate than the blonds for all diseases except dengue, cholera, pneumonia, indigestion, skin diseases, and neurasthenia. In the last disease the comparison is of no value since even among the blonds there was only one admission. For many of the diseases the mixed types showed a higher admission rate than did the blonds.

## SUMMARY OF PART III.

The evidence adduced in this section is conflicting. While sickness was considerably more common among the blonds in the soldier group the reverse is true in the S-C-P-Group. Furthermore, in the latter group the proportion who had never been sick was materially larger among the blonds than among the brunettes. While the statistics were more complete and the number of men considered was much larger for the soldier group, it should be remembered that the period of time spent in the Philippines, and covered by the sick record, was much longer for the S-C-P-Group. Therefore, no conclusion pointing clearly in one direction or the other can be drawn from the statistics compiled in Part III. Of the 21 medical officers who observed the men of the 1910-Group, only one could note any difference in the two types and this officer, Lieutenant Mueller, was of the opinion that the blonds had "suffered from tropical influences somewhat more than the brunettes." He suggested that psychological tests might show deterioration that was not indicated by physical examinations. Unfortunately it was impracticable to make such observations.

## PART IV. SYMPTOMATOLOGY AND DIETARY HABITS FOR THE 1910-GROUP AND FOR THE SCOUT-CONSTABULARY-POLICE-GROUP.

The information dealt with in this part was obtained in the case of the 1910-Group by questions addressed by the medical officers conducting the observations. To each member of the S-C-P-Group a blank form was sent with a request that the printed questions thereon be answered.<sup>12</sup> In setting a value on the following data, it must be remembered that we are dealing mainly with sensations and not with physical signs, and that in case of both officers and men it was well understood why the questions were being asked. The topic of the relative endurance of blonds and brunettes has received not a little popular discussion in the Archipelago, and, therefore, one must consider the possibility that some answers were unconsciously influenced by what the speaker or writer thought should take place.

The individual members of the S-C-P-Group had had continuous tropical service for periods ranging from two to thirteen years, the average being about 5.5 years. For the blonds it was 5.1 years, for the brunettes 5.5 years and for the mixed types 5.6 years. The average Philippine service for the 1910-Group was 18.5 months at the time the questions were asked. The numbers of answers to each question for each complexion type have been reduced to rates per 1,000 of that type in order to facilitate comparison. The replies are shown in Table XXIII, and will be discussed under several subheads.

<sup>12</sup> The data from the Constabulary and the Police were obtained through the courtesy of the Director of the Philippines Constabulary and the chief of the Manila police.

TABLE XXIII.—*Comparative symptomatology in Tropics of blonds and brunettes of Scout-Constabulary-Police-Group and 1910-Soldier-Group.*

Answer number.	Question.	Answer.	Scout-Constabulary-Police-Group.						1910-Soldier-Group.			
			186 blonds.		147 brunettes.		235 mixed types.		323 blonds.		315 brunettes.	
			Number.	Rate per 1,000.	Number.	Rate per 1,000.	Number.	Rate per 1,000.	Number.	Rate per 1,000.	Number.	Rate per 1,000.
1	Have you ever had sunstroke or heat exhaustion?	Yes	7	38	4	27	14	60	16	50	14	44
2	Do you enjoy tropical service? -----	No	12	65	8	54	27	115	123	381	118	375
3		Yes	174	935	139	946	208	885	200	619	197	625
4		No	27	145	16	109	41	174	79	245	76	241
5	Do you feel as well in the Tropics as at home?	Same	145	780	115	782	168	715	230	712	228	724
6		Better	12	65	16	109	26	111	14	43	11	35
	In Tropics do you suffer from—											
7	Insomnia? -----	Yes	13	70	5	34	20	85	14	43	21	66
8	Anorexia? -----	Yes	14	75	9	61	17	72	18	56	20	63
9	Indigestion? -----	Yes	31	167	26	177	45	191	23	71	24	76
10	Diarrhœa? -----	Yes	8	43	9	61	16	68				
11	Palpitation of the heart? -----	Yes	9	48	12	82	12	50	12	37	14	44
12	Sore eyes? -----	Yes	14	75	8	54	19	81	15	46	11	35
13	Loss of memory? -----	Yes	51	274	33	224	65	277	29	90	34	108
14	Do you lose weight in Tropics? -----	Yes	41	220	32	218	49	209				
15	Do you gain weight in Tropics? -----	Yes	64	344	52	354	89	379				
16	Does direct sunlight affect you unpleasantly?	Yes	54	290	41	279	73	311	72	223	70	222
	In the sunlight do you suffer from—											
17	Vertigo? -----	Yes	9	48	18	122	20	85	39	121	30	95
18	Headache? -----	Yes	35	188	22	150	41	174	48	149	44	140
19	Nausea? -----	Yes	4	22	3	20	2	9	11	34	5	16
20	Vomiting? -----	Yes							4	12	3	10
21	Photophobia? -----	Yes	55	296	45	306	87	370	70	217	64	203
22	Excessive thirst? -----	Yes	20	108	13	88	30	128	43	133	36	114
23	Excessive redness of face? -----	Yes							40	124	26	83
24	Shortness of breath? -----	Yes	18	97	11	75	13	55				
25	Do you suffer from lassitude on arising?	Yes	23	124	17	116	47	200	47	146	47	149
26	Are you irritable in the Tropics? -----	Yes	51	274	45	306	92	391	44	136	52	165
27	Are you depressed in the Tropics? -----	Yes	21	113	22	150	29	123	41	127	40	127
28	Do you take a siesta regularly? -----	Yes	39	210	38	259	66	281	146	452	174	552
29	How do your dietary habits compare with those at home?	Same	145	780	121	823	186	792	276	854	273	866
30		Eats less	15	81	13	88	33	140	33	102	25	79
31		Eats more	6	32	5	34	4	18	10	31	12	40
32		Unknown	20	108	8	54	12	50	4	12	5	16

*Sunstroke and heat exhaustion.*—This question covered the whole period of the man's life, and many of the cases occurred in America. In the S-C-P-Group the rate for sunstroke and heat exhaustion was higher for the blonds (38 *per mille*) as compared with the brunettes

(27 *per mille*), but was a great deal higher still for the mixed types (60 *per mille*). In the 1910-Group the rate was also higher for the blonds, but the difference was less marked than in the S-C-P-Group, 50 as compared with 44 *per mille*. In considering the figures for the S-C-P-Group it must be borne in mind that the total number of cases was very small, only 7 for the blonds and 4 for the brunettes, so the element of chance may assume very large proportions.

*Enjoyment of tropical service.*—In the 1910-Group there was no material difference, the rates of those who did not enjoy such service being 381 for the blonds and 375 for the brunettes. In the S-C-P-Group the difference was more marked, 65 *per mille* of the blonds not enjoying the Tropics as compared with 54 *per mille* of the brunettes. However the number of men from the mixed type who did not like such service was far higher than among the blonds, 115 per 1,000. That a much greater proportion of the 1910-Group, as compared with the S-C-P-Group, should dislike the service is natural when it is recalled that the former were enlisted men serving in the Philippines largely from necessity, while the latter were officers and policemen who had elected to reside in the Archipelago, in most cases after having had some preliminary experience with its climate.

*Feeling of well-being in the Tropics.*—The proportion of soldiers in the 1910-Group who did not feel as well in the Philippines as at home showed no material variation for the blonds and for the brunettes, 245 *per mille* for the fair and 241 for the dark complexioned. In the S-C-P-Group the difference was much more marked, 145 per 1,000 of the blonds not feeling as well as in America and only 109 per 1,000 of the brunettes. But here again the mixed types suffered more severely than the blonds, 174 *per mille* of them failing to feel as well as in the homeland. In the 1910-Group the number of blonds who felt better than in America was larger than the corresponding number of brunettes (43 as compared with 35 *per mille*), but in the S-C-P-Group the conditions were reversed, 109 per 1,000 of the brunettes feeling better as compared with only 65 per 1,000 of the blonds. However, the actual numbers of men in this class were small in both groups. The numbers who felt the same here as at home were practically equal for the blonds and for the brunettes in the S-C-P-Group and in the 1910-Group.

With reference to the special symptoms complained of, the actual figures can best be seen in Table XXIII, and it will be sufficient to state here that in the S-C-P-Group the incidence of insomnia, anorexia, sore eyes, and loss of memory was considerably more marked for the blonds while in the 1910-Group the reverse was the case for all except eye troubles. In both groups indigestion, palpitation of the heart, and diarrhoea were more common among the brunettes. It is interesting to

note that for each of the above 7 symptoms, except anorexia, the incidence *per mile* in the S-C-P-Group was higher for the mixed types than for the blonds.

*Influence of direct sunlight.*—In both groups the number *per mille* of blonds who stated that direct sunlight affected them unpleasantly was slightly greater than that of the brunettes, but the differences were immaterial. Again it happened that the mixed types who made complaint were in excess of the blonds. The special symptoms asked about: namely, vertigo, headache, nausea, vomiting, photophobia, excessive thirst, and excessive redness of the face, were all somewhat more common among the blonds than among the brunettes of the 1910-Group, while in the S-C-P-Group the results were similar except for photophobia and vertigo, the former being slightly and the latter two and one-half times more common among the brunettes. Several of these symptoms were of more frequent occurrence among the mixed types than among the blonds.

*General symptoms.*—Lassitude on arising in the morning was slightly more common among the brunettes of the 1910-Group and among the blonds of the S-C-P-Group, but in this latter group the mixed types were much more affected than the blonds. Both irritability and depression were equally common or more common among the brunettes than among the blonds in each group. Both of these sensations were far more frequent among the mixed types than among the blonds of the S-C-P-Group.

*Dietary and siesta habits, and maintenance of weight.*—The numbers per thousand who ate the same amount and kind of food as at home was slightly less for the blonds than for the brunettes in both groups. In the 1910-Group increased consumption of food in the Tropics was more common among the brunettes, while in the S-C-P-Group there was no appreciable difference. The numbers of men *per mille* in the S-C-P-Group who lost weight were equal for the two complexion types, and there was no material difference in the numbers of those who gained weight. In other words complexion did not influence the weight in the S-C-P-Group, and it has been shown in Tables V and VI that the same was true for the 1909-Group and the 1910-Group. In both groups the siesta habit was very much more frequent among the brunettes. For the mixed types it was even more common than for the brunettes.

#### SUMMARY OF PART IV.

Summing up the subjective evidence contained in Table XXIII it may be said that for the 1910-Group, with its 18.5 months of tropical service, the differences are so slight and so variable for the two types that no clear distinction can be made out in the climatic effects produced on the blonds and on the brunettes. In the case of the S-C-P-Group,



with its 5.5 years of Philippine service, the results are inconclusive. On most of the points the advantage seems to be with the brunettes, but on a few the reverse is the case. It is interesting to note that the men of mixed type, who stand intermediate between blonds and brunettes, appeared to suffer from the deleterious influence of the tropical climate more markedly, for nearly every point investigated, than did the individuals of the blond type. This latter fact suggests that some factor other than complexion (possibly chance), may have had a hand in moulding the results in the S-C-P-Group.

PART V. RELATIVE PROPORTIONS OF BLONDS AND BRUNETTES AMONG SOLDIERS INVALIDED HOME, AND IN THE SCOUT-CONSTABULARY-POLICE-GROUP, AS COMPARED WITH THE PROPORTIONS OF THE SAME TYPES AMONG 10,072 SOLDIERS.

As a standard for comparison we carefully examined 10,072 enlisted men of the United States Army in the Philippines during the years 1909, 1910, 1911, and divided them into 3 complexion types, blond, brunette, and mixed, using the classification referred to just below Class VI under "Sources of Evidence." The results are shown in Table XXIV.

TABLE XXIV.—*Comparative number of blonds, brunettes, and mixed types among 10,072 soldiers (1909 to 1911).*

	Blond.	Brunette.	Mixed type.
Actual number .....	2,403	2,073	5,596
Rate per 1,000 men .....	238	206	556
Rate per 100 blonds .....	100	86	233

In the last line of Table XXIV the actual numbers have been reduced to a percentage basis for subsequent comparison with other groups of men and it is seen that for each 100 blonds there were 86 brunettes and 233 of the mixed type.

SOLDIERS INVALIDED HOME.

The figures in Table XXIV may be taken as representing the average proportions of the 3 types among the enlisted personnel of the Army serving in the Philippines at the time of these observations. If the climate be more harmful to the blonds than to the brunettes we should expect that the proportions of incapacitated blonds to incapacitated brunettes would be greater than the ratio of 100 to 86. To determine if such were the case, we have carefully inspected during the last eighteen months all soldiers invalided home from the Philippines and the results, giving actual numbers and rates per 1,000 men, are shown in Table XXV. The mean strength of the command from which this invaliding occurred was approximately 11,678 men.

TABLE XXV.—*Diagnoses of men invalided home, arranged by complexion types.*

Diagnoses.	Blonds.		Brunettes.		Mixed types.		Total, all types.	
	Num- ber.	Rate per 1,000 men.	Num- ber.	Rate per 1,000 men.	Num- ber.	Rate per 1,000 men.	Num- ber.	Num- ber.
Nervous diseases:								
Neurasthenia .....	5		10		2		17	
Epilepsy .....	2		4		1		7	
Miscellaneous .....	7		4		3		14	
Total nervous .....	14	368	18	474	6	158		38
Mental diseases:								
Dementia præcox .....	4		9		6		19	
Melancholia .....	1		2		1		4	
Depressional insanity .....			1		1		2	
Insanity, type undeter- mined .....	4				5		9	
Defective mentality .....			5		1		6	
Total mental .....	9	225	17	425	14	350		40
Intestinal diseases:								
Sprue .....	1		1		1		3	
Enteritis, chronic .....	4		8		5		17	
Dysentery, chronic .....			1		1		2	
Diarrhoea, chronic .....	1		1				2	
Ulcer of rectum .....			1				1	
Total intestinal .....	6	240	12	480	7	280		25
Venereal diseases; all forms .....	4	364	5	454	2	182	11	11
Blood and circulatory diseases:								
Valvular lesions .....	1		2		3		6	
Anæmia, pernicious .....	1				1		2	
Anæmia, secondary .....	1				2		3	
Polycythemia .....	1						1	
Phlebitis .....	2						2	
Total blood and circula- tory .....	6	429	2	142	6	429		14
Tuberculosis; all forms .....	22	314	27	386	21	300	70	70
Malaria and its sequelæ .....	2	500	1	225	1	225	4	4
Alcoholism, chronic .....	3	600	1	200	1	200	5	5
Gout and chronic rheumatism .....			3	500	3	500	6	6
Kidney diseases; all forms .....	2	333	4	667			6	6
Pulmonary diseases (except tuberculosis) .....	2	286	3	428	2	286	7	7
Diseases special senses:								
Deafness .....	1				1		2	
Otitis media and externa .....	3		1		3		7	
Retinitis .....	2				1		3	
Total special senses .....	6	500	1	83	5	417		12
Sunstroke .....		0		0	1	1,000	1	1
Wounds and injuries .....	4	191	7	333	10	476	21	21
Miscellaneous diseases .....	4	308	5	384	4	308	13	13
Totals .....	84	308	106	388	83	304	273	273
Rate per 100 blonds .....	100		126		99			

On examining the total numbers of each type invalided home from all causes (which have been reduced to a percentage basis in the last line of Table XXV) one immediately notices that the proportion of mixed types is considerably lower than was the case among the 10,072 men taken as a standard. Turning to the blonds and brunettes it is seen that the ratio is 100 to 126, whereas the ratio of blonds to brunettes among 10,072 soldiers was 100 to 86. In other words while the blonds exceed the brunettes in the general military population the reverse is the case in the total of invalided men. This is strong evidence that the blonds do not suffer unduly from the influence of the climate, but is at variance with the evidence adduced in Part III showing that there is more sickness among the blonds than among the brunettes.

On considering the special causes of incapacity it is seen that tuberculosis heads the list in importance, and shows a larger rate for brunettes than for blonds. In both nervous and mental diseases the rate is much higher for the brunettes. Neurasthenia, which especially has been attributed by some to the influence of the tropical sunlight, was nearly twice as frequent a cause of incapacity for the brunettes as for the blonds, and the same was true for intestinal and kidney diseases. Venereal diseases, gout and rheumatism, pulmonary troubles, accidents, and miscellaneous affections were all higher for the brunettes. Only in circulatory and blood diseases, alcoholism, malaria, and disturbances of the special senses were the blonds the greater sufferers.

We would not argue from such a comparatively small series that the blonds are better able to withstand a tropical climate than are the brunettes, but we do consider that Tables XXIV and XXV indicate that they are *fully as resistant* to the Philippine climate as are their darker skinned companions.

#### RATIO BETWEEN THE THREE TYPES IN SCOUT-CONSTABULARY-POLICE-GROUP.

The members of this group have voluntarily elected to reside in the Philippines, usually after having had some preliminary experience with the climatic conditions. Many of them have been in the Archipelago for twelve or thirteen years and the average length of continuous tropical service is 5.5 years. Nearly all of the Scout officers and the policemen originally came to the Archipelago as enlisted men in the Army, and a good proportion of the Constabulary officers also were drawn from that class. If the climate of the Philippines affected blonds more seriously than brunettes we should expect that after several years' residence the ranks of the blonds would be depleted by death, invaliding, and voluntary departure, and that the ratio of blonds to brunettes would be lower than the same ratio among the enlisted men (Table XXIV) from whom the S-C-P-Group sprang. Such is not found to be the case. Among the 568 men of the S-C-P-Group there were 186 blonds, 147 brunettes, and

235 mixed types. Reducing these to the percentage basis we have, for each 100 blonds, 79 brunettes and 126 of the mixed type. It will be observed that the proportion of the latter type is lower than the Army average (Table XXIV), but that the proportion of blonds as compared with brunettes is higher than the average for enlisted men of the Army in the period from 1909 to 1911 (100 to 79 as contrasted with 100 to 86).

These facts tend to show that in an average tropical service of 5.5 years the relative resistance of the blonds is not so impaired as to lead to a depletion of their ranks disproportionate to that occurring among the brunettes. To refute these deductions it might be argued that the proportions of the three complexion types among the American troops may not have been the same 6, 8, 10 or 12 years ago, at which times many members of the S-C-P-Group severed their connections with the regular Army, and that originally the blonds may have been much in excess of the brunettes in the S-C-P-Group. We have no statistics as to the proportions of the different complexion types in the Army for the period 1898 to 1901 and it is possible that in the earlier part of this period blonds may have been relatively somewhat more numerous, especially among the Western volunteers. However, we do have some statistics gathered in 1902 and 1903 by Woodruff,<sup>(2)</sup> and tabulated on page 215 of his book on Tropical Light.<sup>13</sup> Out of 1,294 soldiers there were 420 blonds, 356 brunettes, and 518 mixed types. Reduced to the percentage basis he found for each 100 blonds, 85 brunettes and 123 of the mixed type. On comparing these figures with those in the last line of Table XXIV it is seen that the blonds were not appreciably more numerous in the Army in 1902-3 than they were in 1909-11, and that they were considerably less numerous than they are at the present time (1911) in the S-C-P-Group.

#### SUMMARY OF PART V.

The ratio of invaliding home is lower for the blonds than for the brunettes. The ranks of the blonds in the S-C-P-Group after 5.5 years' tropical service, have not been depleted, the proportion of the fair complexion type being probably higher in the S-C-P-Group now than it was among the class from which that group was originally drawn. These are strong arguments in favor of the assumption that the blonds are quite as well able as the brunettes to resist the tropical conditions met with in the Philippines at the present time.

<sup>13</sup> Our system of classifying men into blonds and brunettes is the same as that described by Woodruff. His ratio of blonds to brunettes agrees closely with ours, but we find a considerably larger mixed class than he reports.

PART VI. CHARACTER, COURT-MARTIAL RECORDS AND SICK RATES FOR ALCOHOLISM AND VENEREAL DISEASE IN THE 1910-GROUP.

Woodruff<sup>(3)</sup> quotes some figures in support of a theory that the irritation produced by an excessive amount of sunlight may effect the conduct unfavorably and increase the prevalence of crime. If such is the case it is conceivable that misdemeanors would be more frequent among blonds than among brunettes in the Tropics. With a view to investigating this point the following tables have been compiled for the 1910-Group. The first shows the number of trials by courts-martial, the fines and days of confinement resulting therefrom, the military character given the men by the company commanders, and any changes of character occurring while in the Philippines. The other gives the degree of alcoholic consumption and the days on sick report from alcoholism and venereal diseases.

TABLE XXVI.—Comparative character and comparative averages of court-martial trials, confinement and fines for 345 blonds and 343 brunettes, 1910-Group.

Type.	Military character.						Change of character.			Disciplinary measures.		
	Ex-cel-lent.	Very good.	Good.	Fair.	Bad.	No state-ment.	Bet-ter.	Worse.	No change.	Trials num-ber.	Con-fine-ment, days.	Fines, dollars.
Blond -----	207	72	29	9	1	27	4	12	329	0.4	3.9	3.49
Brunette -----	202	73	26	8	0	34	7	8	328	0.4	3.6	3.97

TABLE XXVII.—Comparative consumption of alcohol and comparative numbers of days lost from alcoholism and venereal disease for approximately equal numbers of blonds and brunettes.<sup>a</sup>

Type.	Consumption of alcohol.				Days on sick report from—	
	None.	Slight.	Moder-ate.	Exces-sive.	Alcohol-ism.	Venereal disease.
Blond -----	62	110	138	13	62	5,327
Brunette -----	61	82	163	9	31	5,297

<sup>a</sup> The figures for consumption of alcohol are for 323 blonds and 315 brunettes of the 1910-Group. The days lost on sick report from alcoholism and venereal disease are for 504 blonds and 500 brunettes, all the men in both the 1909-Group and the 1910-Group.

In both these tables the numbers of blonds so nearly equal the numbers of brunettes that the figures have not been reduced to rates per 1,000, since this calculation would not appreciably affect the comparison. As

regards courts-martial and their results, the differences between the two types are immaterial. The numbers of trials are identical, the blonds had an average of 0.3 day more of confinement, but the brunettes received an average of 0.48 dollar more fines. The classifications of the two types according to military character agree as closely as could be expected in groups of this size. As regards change of character an equal proportion of each type underwent no alteration, but of the 16 blonds and 15 brunettes whose character did change, 12 of the blonds deteriorated as compared with 8 of the brunettes. However, the number who changed is so small that it would be unsafe to make deductions therefrom.

In Table XXVII it will be seen that the number of abstainers was practically the same in both types and that the blonds had a larger number of slight drinkers and fewer moderate ones. The number of excessive drinkers was greater among the blonds than among the brunettes (13 as compared with 9). There were 18 admissions for alcoholism and 62 days lost among the blonds as compared with 6 admissions and 31 days lost among the brunettes. The days on sick report from venereal diseases were practically equal for the two complexion types.

#### SUMMARY OF PART VI.

In summing up it can be said that there was no appreciable difference in behavior between the blonds and the brunettes except in regard to stimulants, the excessive use of alcohol being somewhat more common among the blonds. However, too much weight should not be given to this last conclusion in view of the small numbers of persons who indulged to excess.

#### PART VII. RELATIVE FREQUENCY OF OCCURRENCE OF SUNSTROKE AMONG BLONDS AND BRUNETTES IN THE UNITED STATES.

The exact causation of sunstroke and heat exhaustion remains in doubt in spite of the many theories advanced by eminent observers. Among these theories may be mentioned that advocated by Maude of the British Army, who considered that sunstroke was due to the action, upon the head, of the actinic rays of the solar spectrum and believed that insolation could be prevented by inserting in the headdress a layer of material impervious to these rays. He employed a red hat lining. In connection with our work on the influence of climate on blonds and brunettes it was desired to obtain statistics as to the complexion type of men suffering from insolation. Such figures could not be obtained in the Philippines, because heat exhaustion is rare and true sunstroke practically unknown in the Archipelago. Therefore, statistics were gathered from the large cities in the United States through the courtesy of the

officials of the institutions enumerated in footnote 6. The results are shown in Table XXVIII.

TABLE XXVIII.—*Numbers of each complexion type among 367 persons suffering from insolation in the United States.*

Group.	Year.	Blonds.	Brunettes.	Mixed types.	Total.
I	1910	9	48	9	66
II	1911	4	65	11	80
III	1911	72	70	87	229

In Groups I and II the separation into complexion types was made by the physicians at the various hospitals, our system of classification having been furnished them. It will be noticed that they placed extremely few in the blond type, perhaps assigning to that class only the most conspicuous examples of blondness. In Group III the physicians were requested to fill out for every case of insolation a printed form which contained among other things the following complexion-type table.

Color of hair.	Color of eyes.	Complexion.
Flaxen.	Light blue.	Light.
Red.	Medium blue.	Ruddy.
Sandy.	Dark blue.	Fair.
Light brown.	Gray.	
Medium brown.	Brown.	Medium.
Dark brown.	Black.	Dark.
Black.		

The physicians prepared one of these blank forms for every patient suffering from insolation, and made a check-mark after the appropriate word in each of the three columns of the complexion-type table. The completed forms were then sent to us and, following the rule used in our work among the soldiers, we classed as blonds those who had the three check-marks above the dividing line, and as brunettes those where all the check-marks were below the line. If some marks were above and some below the man was placed in the class composed of mixed types.

We received 229 of these cards and they are recorded in Table XXVIII as Group III. There were 72 blonds, 70 brunettes, and 87 mixed types. Reduced to a percentage basis, for each 100 blonds there were 97 brunettes. As shown in Table XXIV the proportions of blonds to brunettes among our 10,072 soldiers was as 100 to 86. Therefore, it is clear that the ratio of brunettes suffering from the effects of the sun in the United States was materially higher than the ratio of the same type among 10,072 American soldiers.

## SUMMARY OF PART VII.

Unfortunately we have no exact statistics to show what may have been the proportions of the two complexion types in the cities under consideration. Woodruff states that the blonds are less numerous in the cities than in the country. Our Army is recruited from both urban and rural sources and it is doubtful if the figures for complexion type in the cities differ very much from those found in the military service. If this be true, then it is obvious from a study of Group III that the blonds in the United States were not quite as subject to insolation as were the brunettes. If any deductions are to be drawn from Groups I and II, they would be that the harmful effects of the sun are very much less manifest among the fair skinned individuals.

PART VIII. DISCUSSION OF CLIMATIC INFLUENCES AND PIGMENTATION:  
GENERAL SUMMARY: CONCLUSIONS.

It seems to us by no means proved that the pigmentation of tropical races and the tanning of Caucasians is a protective effort on the part of nature against the chemical activity of sunlight. Several other explanations suggest themselves, but will not be discussed here. The integument of the negro is able to radiate heat more readily than that of a white man, but this advantage is least manifest when most needed, namely in direct sunlight, where the superior radiating power of the black skin is more than counterbalanced by the facility with which the dark colors absorb thermic rays. However, it does seem proven that on the living subject the brown or black skin, when exposed to the sun, is always slightly cooler than the skin of a white man.<sup>(4)</sup> This apparent anomaly is explained on the ground that the cooling effects produced by evaporation are more marked in the case of the dark races, because of anatomical differences in the skin. Daubler states that the negro has sweat glands which are larger and better developed than those of the Caucasian. Some claim that the number of glands in a given area is greater. Aron considers that the brown skin is cooled more efficiently because the perspiration is secreted more evenly, the evaporation is complete, and the waste, due to the sweat dropping off, is avoided. The above conditions, taken together with the fact that the working native wears very little clothing, place the pigmented native in a better position than the Caucasian as regards the heat regulation of his body in the Tropics.

The advocates of the theory that certain deleterious effects noted in the Tropics are due to the chemical rays of the sunlight, point to sunburn as an evidence of injury produced by actinic rays and maintain



that pigmented skin will absorb these harmful waves.<sup>(2) (7)</sup> The pigmentation following sunburn is considered a conservative effort on the part of the organism. The supporters of the actinic theory advocate the use of protective clothing, a red, orange-red, or black layer being recommended. Some advise a tinfoil lining for the headgear. Now it is a matter of general observation that the covered portions of the body do not become tanned or sunburned when ordinary clothing is worn. If sunburn and tanning are due to actinic rays, and if the usual clothing is able to protect the skin from their effects, it seems to us reasonable to assume that the same clothing will protect the body as a whole from the effects of these rays. This argument of course does not take into consideration that quantity of rays which may enter through the face and hands, but no one, as far as we are aware, has recommended covering these parts. Therefore, it seems probable on theoretical grounds that ordinary clothing gives sufficient protection, and the result of an extensive practical experiment by the Board<sup>(10)</sup> supported this view by showing that no benefit resulted from the use of orange-red hat linings and underwear.

Recently Aron<sup>(4)</sup> has shown that monkeys, when exposed to the direct rays of the sun in Manila, quickly develop a high temperature and die in one or two hours. Monkeys exposed under similar conditions, while at the same time a strong current of air from an electric fan blew over their bodies, did not suffer any discomfort. Of course the amount of chemical rays falling on the animals was identical in the two cases. The inability of monkeys to stand sun exposure is considered by Aron to be due to the fact that these animals possess no sweat glands, and consequently have only a limited power of thermic regulation. Therefore, hyperpyrexia occurs as a result of the absorption of solar heat rays. No rise of temperature and no ill results occurred when monkeys' heads were exposed for several days while their bodies were protected from the sun. Aron concludes that "hyperthermia alone must be regarded as the true cause of the death and of the injurious effects brought about by the radiation of the sun." While Aron was working at the Bureau of Science in Manila on the thermic factor in the tropical sunlight, Freer<sup>(1)</sup> and others have been engaged in the investigation of the chemical side of the problem without producing any results which would show that the actinic rays of the spectrum were distinctly detrimental to man.

The researches of Freer and Aron, the results of the orange-red clothing test by Phalen<sup>(10)</sup> of this Board, the observations of Wickline<sup>(9)</sup> on blonds and brunettes and our own work on the same subject render it

very doubtful in our minds whether chemical rays of the sunlight and complexion types of Caucasians are factors of any importance in tropical pathology. The experiences of Gorgas in Panama, the reports of various other workers from many countries, and our own general observations in the Philippines, all lead us to the conclusion that the main cause of tropical deterioration, as seen in the past, was infection of the skin, blood, intestines, and other regions, with those parasites which are more common in the Tropics than in the temperate zone. The vast improvement in the health conditions in Cuba, Panama, and the Philippines, which has followed action based on such a parasitic theory, is strong evidence in favor of our assumption. The enervating effects of continued heat and humidity doubtless play some part, especially in the direction of discouraging out-door exercise. Nostalgia, isolation, and monotony, and the excessive use of alcohol resulting therefrom, are factors of considerable importance. To account for what is observed in the Philippines it does not seem to us necessary to call in the hypothetical action of the actinic rays in the sunlight, nor do we think that there is any adequate evidence that such action is a factor in tropical morbidity and deterioration. It appears that the men who spend much time actively engaged out of doors in the Philippines are the ones who remain in the best health. Those who suffer most from nervous affections are the women, and they pass practically all their time in the shade. The situation is well described by Castellani and Chalmers who state that "the basis of the largest proportion of illness and death in the Tropics is bad sanitation and not climatic influences." (7)

The direful effects of the Philippine climate, which have been so vividly depicted by Woodruff, relate to the earlier days of the American occupation and are not seen at the present time. It is our belief that these unfortunate occurrences were due chiefly to infections resulting from the poor hygienic conditions unavoidable in the early campaigns. It does not seem that any effort is now made to spare officers or men from exposure to the sunlight, yet the morbidity and the mortality continually decrease. Affections of the nervous system, including insanity, are among the diseases considered by Woodruff to be particularly likely to occur in the Tropics, as a result of excessive light stimulation, and he bases his argument on statistics from the reports of the Surgeon-General covering the calendar years 1901 and 1902. To determine if the same argument holds good at the present time, the figures for the last seven years for which statistics are available have been compiled from the reports of the Surgeon-General of the Army and are shown in Table XXIX.

TABLE XXIX.—*Relative admission rates for insanity and for nervous diseases in the Army serving in the Philippines and in the United States, 1903 to 1909.*

Calendar year.	Admission rate per 1,000.			
	Insanity.		Nervous diseases.	
	Philip- pine Islands.	United States.	Philip- pine Islands.	United States.
1903 <sup>a</sup> .....	1.05	1.02	22.67	21.77
1904.....	1.75	1.71	20.34	22.10
1905.....	1.45	1.61	20.53	19.49
1906.....	2.02	1.33	19.55	19.47
1907.....	1.88	1.79	19.32	20.15
1908.....	1.09	1.58	19.30	18.44
1909.....	1.56	1.63	16.82	16.61

<sup>a</sup> Figures for the Philippines in 1903 include also those for troops serving in China.

These figures show that there is no constant or essential difference between the admission rates for insanity and nervous diseases in the United States and in the Philippine Islands. In many instances the ratio is higher in the United States. Tables XXI, XXII, and XXV indicate how small a part neurasthenia now plays in the morbidity of Americans in the Philippines. Yet the sunlight is the same as in the period from 1898 to 1902, but the hardships, the bad sanitation, the poor food, the isolation, and the nostalgia have been largely remedied. As stated before, we believe that the most of the neurasthenia here is among the women, who rarely go out in the sun. Among the cases of insanity classified in Table XXV, a very large proportion were considered to have existed at date of enlistment, and not to have been due in any way to the climatic influences of the Philippines.

#### GENERAL SUMMARY.

It is well known that heat and humidity in an experimental chamber, and in the absence of light, can produce symptoms similar to those occurring in milder degree among residents of the Tropics. We think it probable that these two factors, combined with infections, nostalgia, and monotony, account for most if not all of the injurious effects seen in tropical lands. To explain the conditions met with in the Philippines there seems to be no need for invoking the aid of the actinic rays of the solar spectrum. Protection against these rays by orange-red clothing was of no benefit. It is by no means proved that pigmentation *per se* is beneficial in the Tropics. In our investigations of blonds and

brunettes the evidence was conflicting, some facts being in favor of the fair and others in favor of the dark complexioned men. This is what would be expected if there were actually no differences between the two types as regards their resistance to tropical influences. From a consideration of all the data it appears that blonds are quite as well able as brunettes to withstand the influences of the Philippine climate for a period of two years and probably for a period of five and one-half years. In case of residence beyond the latter period we are not in a position to express an opinion based on any extensive personal observation.

In concluding we wish to acknowledge our indebtedness to the officials of the Division Hospital in Manila for affording the opportunity to examine the patients invalided home; to the Director of the Philippines Constabulary and the chief of the Manila police for collecting statistics from their subordinates; to the superintendents of the institutions in the United States who classified their cases of insolation; and especially to the medical officers named in footnotes 3 and 5, who, by their enthusiastic and conscientious work, made it possible to obtain the data considered in Part II of this report.

#### CONCLUSIONS.

1. Exact observations continued for a period of one year on large numbers of blonds and brunettes in the military service showed no constant or material differences for the two complexion types.

2. The amount of sickness occurring in the Philippines was larger among the blonds in the soldier group and among the brunettes in the Scout-Constabulary-Police-Group. In the latter group the proportion of men who had never been sick was much larger for the blond type.

3. As regards disagreeable symptoms referable to climate the evidence was conflicting, but on the whole the blonds suffered more than the brunettes.

4. Among the soldiers invalided home the brunettes were in much larger proportion than they were in the Philippine forces as a whole.

5. In the Scout-Constabulary-Police-Group, which had an average of 5.5 years of tropical service, the proportion of blonds as compared with brunettes was probably as high as it ever had been.

6. The military conduct of the blonds appeared to be as good as that of the brunettes except perhaps in regard to alcoholism.

7. In the United States the relative incidence of insolation was probably slightly higher among the brunettes than it was among the blonds.

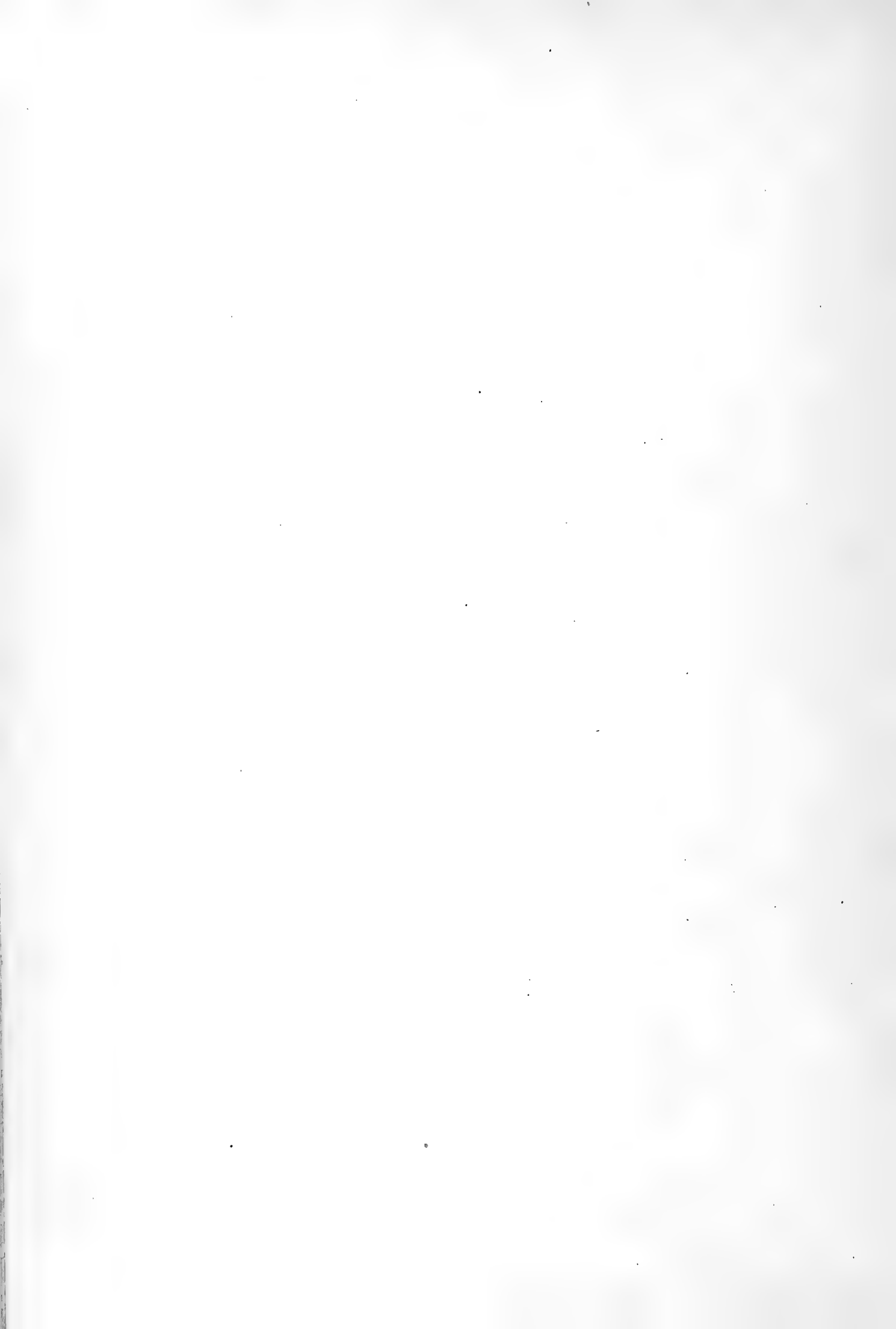
8. On the whole the blonds seemed fully as able as the brunettes to withstand Philippine service for a period of two years, and probably as able for a period of five or six years.

9. The incidence of nervous diseases and insanity in the Army during the last seven years has not been different in the Philippines from what it was in the United States.

10. It is doubtful if the actinic component of the sunlight is a factor in tropical morbidity and deterioration.

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## ILLUSTRATION.

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Map of Philippine Islands, showing locations where the observations on the  
blonds and brunettes were carried out.

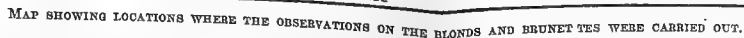
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1.  $\mathcal{P}^{\text{int}} = \{P \in \mathcal{P} \mid P \text{ is internal}\}$   
 2.  $\mathcal{P}^{\text{ext}} = \{P \in \mathcal{P} \mid P \text{ is external}\}$











# A STUDY OF THE SYSTOLIC BLOOD-PRESSURE AND THE PULSE RATE OF HEALTHY ADULT MALES IN THE PHILIPPINES.

BASED ON 6,847 BLOOD-PRESSURE READINGS ON 1,489 INDIVIDUALS, AND AN EQUAL NUMBER OF PULSE COUNTS ON THE SAME PERSONS.<sup>1</sup>

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By WESTON P. CHAMBERLAIN.<sup>2</sup>

(*From the United States Army Board for the Study of Tropical Diseases.*)

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## INTRODUCTION.

During the period from January 1, 1909 to September 30, 1911 the Board for the Study of Tropical Diseases carried out in the Philippines two extensive series of observations, one to determine whether Americans of the blond type suffered more than the brunettes from the deleterious influences attributed to the tropical climate<sup>(1)</sup> and the other to discover whether the wearing of orange-red underclothing, which obstructs the passage of the actinic rays of the solar spectrum, was of any benefit to white soldiers serving in the Archipelago.<sup>(2)</sup> The compiling and analyzing of the data was done by the Board. A part of the laboratory examinations were made by the Board, but the bulk of the observations were carried out by 24 medical officers of the Army who were specially detailed for the purpose and who worked under the supervision of the Board. As a result of these two series of observations an immense amount of data was collected, which was of value not only in settling the points for which the work was instituted, but also as affording a basis for the study of special features of the physiological activity of the Caucasian when living in the Philippines.

The present report will deal with the subject of blood-pressure in the Tropics and with the associated pulse rate. During the above mentioned observations 6,128 blood-pressure readings and an equal number of syn-

<sup>1</sup> Published with permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> Weston P. Chamberlain, major, Medical Corps, United States Army, president of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

chronous pulse counts were made on 1,042 white men.<sup>3</sup> Five hundred and fifty-two blood pressure readings and 200 pulse counts were made on 386 Filipinos, most of this work having been done by the Board, but a part by some of the officers mentioned in footnote 3. When the number of observers, all trained in laboratory methods, is considered, it will be obvious that the influence of the personal equation in this work has been reduced to a minimum. The great number of observations enables us to avoid the errors inherent in a small series of cases.

For convenience in reference the men examined in the orange-red underwear tests will be denominated the 1909-Group and those examined during the blond-brunette observations will be referred to as the 1910-Group.

#### CLASS OF PERSONS EXAMINED.

All of the Caucasians examined were American soldiers, representing a good class of healthy young adults. Diseased men were barred by the stringent physical examination required at the time of enlistment. Furthermore, all the men in both groups were looked over just before the above mentioned observations began and any who appeared to be in ill health were excluded. Very few of the individuals were over 40 or under 20 years of age and none were below 18 years.

The Filipinos examined were from various tribes. One hundred were soldiers of the Philippine Scouts and an equal number were from the Philippines Constabulary. The remainder of the group was made up of laborers, servants, and convicts. With the exception of a few of the convicts, all were under 42 and the majority were less than 30 years of age. A series of 20 Igorots living at Baguio (elevation 1,500 meters) was also examined, but these are not included in the general averages for Filipinos. Both the whites and the great bulk of Filipinos belong to a class of men of good physical development and constantly engaged in vigorous out-of-door work, with no special effort taken to protect them from the sunlight.

#### CLIMATE AND GEOGRAPHY.

Only brief reference will be made to the climate and geography of the Archipelago where these observations were made, because the subject is dealt with quite fully in another report of the Board.<sup>(1)</sup> The islands on which the blood-pressure readings were taken extended in latitude from 19° north to 6° north. Except on high mountains the climate is everywhere tropical with a maximum recorded temperature in Manila of 37°.8 C. (100° F.) and minimum of 15° C. (59° F.).

<sup>3</sup> The medical officers who participated in the making of these observations on pulse and blood-pressure were the following: Majors C. C. Collins and Roger Brooke, jr.; Captains C. D. Cowles, G. L. McKinney, H. A. Philips, J. R. Barber, Mahlon Ashford, E. G. Huber, H. M. Snyder, and W. L. Hart; and First Lieutenants Armin Mueller, M. C. Stayer, L. C. Garcia, and C. E. Fronk.

The blood-pressure work on white men was done at 7 points, Camp Stotsenburg, Fort William McKinley, Camp Jossman, Warwick Barracks, Torrey Barracks, Pettit Barracks, and Augur Barracks. Part of the natives were examined at these places, but the majority were tested at Camp Gregg, Corregidor Island, and in Manila. All of the 10 places above mentioned are located on or close to the coast-line and but little above sea level with the exceptions of Camp Stotsenburg and Camp Gregg which are in the interior at altitudes not exceeding 200 meters. The climate at these two last posts does not differ materially from that at the other stations nearer the sea.

#### BLOOD-PRESSURE APPARATUS AND METHOD OF USE.

The instrument used for all of the tests was the portable form of Doctor Cook's modification of the Riva-Rocci apparatus. The original instrument devised by Doctor Cook had a 4.5-centimeter armlet, which width, according to the experience of most observers, gives readings that are too high.<sup>(3)</sup> The results are more markedly exaggerated, above what they should be, when the pressure is considerably above normal or when the circumference of the arm is great. Erlanger, v. Recklinghausen, Gallavardin, and Janeway all advocate a 12-centimeter cuff. The instruments with which our routine observations were made had an armlet 8 centimeters in width. In order to reduce the readings made with this 8-centimeter cuff to the basis of a broad armlet we made a series of 140 comparative observations on 60 white men and 288 observations on 120 Filipinos, using with Doctor Cook's apparatus one cuff of a width of 8 centimeters and another of 12.5 centimeters (5 inches). We found that with the 12.5-centimeter cuff the recorded pressure on the average was lower by 8 millimeters for white men, and by 6 millimeters for Filipinos, than was the case when the 8-centimeter armlet was employed. The difference between the results in the two races probably was due to an average smaller circumference for the native arms. In the tables which follow the average readings have all been reduced to the basis of a 12.5-centimeter armlet by deducting 8 millimeters for the whites, and 6 millimeters for the natives, from the averages of the original observations made with the 8-centimeter armlet.

It may be argued that a constant deduction of 8 millimeters would give inaccurate individual results for the very high and for the very low pressures. Even if this be so it would not affect the average figures given in our tables since they are in all cases the average of individual readings on great numbers of men and the 8- or 6-millimeter deduction is the mean difference in a large series of men of the same race, occupation, and physical type.

We applied the cuff to the upper arm and for determining the pressure used as a criterion the return of the pulse wave in the radial artery. Nearly all of our observations were taken with the soldier in the sitting posture. For some individuals the readings were made when the men were reclining, but the numbers so recorded are so small in comparison with the total number of men observed that it would not materially affect the averages even if it be granted that there is a constant slight difference between the readings in the two postures. Erlanger and Hooker found the pressures about the same sitting or lying and Janeway considers the postural variations to be insignificant.<sup>(3)</sup> Our observations

were made at various hours between 8 a. m. and 4 p. m. Those observations on white men which are included in the general averages were in many cases taken after the soldier had been performing his usual military duties, such as drill or fatigue. In a special group, not included in the general averages and which will be described later, the blood-pressure readings and pulse counts were made as soon as possible after vigorous exercise. In the case of the natives all pressures were taken when the men had no exercise immediately preceeding the observations.

The observations on the 1909-Group continued for ten months, blood-pressure readings being taken for each man on 4 occasions during that period, the time between readings being about three months. In the 1910-Group, 5 blood-pressure observations were made on each individual, 1 at the commencement of a 12-month period, 1 at its end and the 3 others at quarterly intervals. In Tables II, III, IV, V, and XIII the average readings are made up from the combined 4 or 5 quarterly observations taken on each man and so represent the *mean annual blood-pressure*. Therefore, it is obvious that the disturbing influence of such factors as excitement, alcoholism, temporary indisposition, the ingestion of food, or the taking of exercise, is reduced to a minimum and that the average for each individual must represent very accurately his normal blood-tension.

#### STANDARD OF NORMAL BLOOD-PRESSURE IN TEMPERATE CLIMATES.

The wide variations in normal blood-pressure which have been recorded by different writers are probably due largely to the use of armlets varying in width. Janeway states that in young adult males the systolic pressure ranges from 100 to 130 millimeters of mercury when a 12-centimeter armlet is used. Gallawardin<sup>(4)</sup> considers the ordinary mean to lie between 110 and 120 millimeters. A very valuable series of statistics was published in 1910 by Woley.<sup>(5)</sup> He analyzed the blood-pressures of 1,000 supposedly healthy individuals, using a 12.5-centimeter (5-inch) cuff applied to the arm when the subject was in the sitting posture. He found the average systolic pressure for all males to be 127.5 millimeters and for all females 120 millimeters. Classifying his 1,000 cases according to age he obtained the following results:

TABLE I.—Woley's average systolic blood-pressures for 1,000 healthy persons in the United States. (12.5-centimeter armlet.)

Range of age.	Average pressure.	Range of age.	Average pressure.
<i>Years.</i>	<i>mm.</i>	<i>Years.</i>	<i>mm.</i>
15 to 30	122	40 to 50	130
30 to 40	127	50 to 60	132

Faught considers the average normal systolic pressure at the age of 20 to be 120 millimeters.<sup>(9)</sup> Bachmann<sup>(7)</sup> examining healthy students



in Philadelphia with a 10-centimeter cuff found an average pressure of 114.3 millimeters for a series of 10 boys ranging from 15 to 20 years of age; 119 millimeters for 53 men ranging from 21 to 30 years; and 120 for 9 individuals ranging from 31 to 40 years.

Most of the older statistics for blood-pressure on healthy persons are based on readings made with narrow, constricting bands like the 5-centimeter armlet used with the early Riva-Rocci apparatus. Such figures are always too high.

*The figures given above indicate that in the temperate zone and with a wide armlet the mean blood-pressure for healthy men from 15 to 30 years of age should be looked for between the limits of 115 and 120 millimeters, certainly not above 122 millimeters.*

INFLUENCE OF TROPICAL CLIMATE ON BLOOD-PRESSURE AND PULSE RATE.

The average blood-pressure with the 12.5-centimeter armlet, based upon 5,368 readings on 992 American soldiers serving in the Philippines, was 115.6, and the pulse rate for a like number of observations on the same men was 81 per minute. These men ranged in age from 18 to 50 and the average was 26.6 years. The average length of their present tour of tropical service was about eleven months at the *beginning* of the year during which the men were under observation. Table II shows the details of these observations.

TABLE II.—Average systolic blood-pressures and pulse rates, based on 5,368 observations of each which were made on 992 American soldiers serving in the Philippines; arranged according to age. (12.5-centimeter armlet.)

Age period, years.	Average age, years.	Number of men showing pressures from—							Total number of men.	Average pressure.	Average pulse rate.
		91 to 100 mm.	101 to 110 mm.	111 to 120 mm.	121 to 130 mm.	131 to 140 mm.	141 to 150 mm.	151 to 160 mm.			
18 to 20	19.4	1	12	13	8	1	1		36	mm. 115.0	78
20 to 25	22.8	32	156	165	87	22	5	2	469	114.3	82
25 to 30	27.2	16	73	108	70	13	3	3	286	115.9	81
30 to 35	32.6	2	34	42	23	7	1		109	116.7	80
35 to 40	37.5		9	24	14	8	3		58	120.5	81
Over 40	43.1	2	3	17	7	2	2	1	34	119.6	79
Totals or averages	26.6	53	287	369	209	53	15	6	992	115.6	81

It will be seen from the above table that the blood-pressures for the ages from 18 to 30 average 115 millimeters, which is 7 millimeters lower than Woley found and 3 millimeters lower than Bachmann found for the same age period in the United States. However, it is exactly midway in the normal range set by Gallavardin and Janeway for temperate

climates. For the period from 30 to 40 years our average was 118 millimeters, which is 9 millimeters lower than Woley's but only 2 millimeters lower than Bachmann's experience for the same ages. The pulse rate for all ages was 9 beats above the accepted normal for temperate climates.

INFLUENCE OF LENGTH OF TROPICAL RESIDENCE ON BLOOD-PRESSURE  
AND PULSE RATE.

Since the number of men who had lived over a year in the Philippines was considerably greater for the 1909-Group than it was for the 1910-Group these two groups have been tabulated separately according to length of tropical service in Tables III and IV, as well as combined in Table V. The average age of the men in the group for each quarterly period of tropical service has also been given because age has a distinct bearing on blood-pressure. As stated above, our complete series of blood-pressure observations consisted of 4 or 5 readings for each individual, evenly spaced through a year, but in the next 3 tables only the *first* of these readings has been considered and the figures in the first column of each of the 3 tables indicate the number of months intervening between the date of arrival in the Philippines and date of the initial blood-pressure reading for each soldier in the sub-group.

TABLE III.—Average systolic blood-pressures and pulse rates for 587 men of the 1909-Group, arranged by length of Philippine residence. (12.5-centimeter armlet.)

Length of tropical residence.	Number of men.	Average pressure.	Average pulse.	Average age.
		<i>mm.</i>		
3 months or less .....	76	110	75	23.8
3 to 6 months.....	14	118	78	26.1
6 to 9 months.....	123	112	76	24.3
9 to 12 months.....	232	118	89	24.0
12 to 15 months.....	47	118	77	24.6
15 to 33 months.....	26	122	79	30.0
33 to 36 months.....	22	119	83	30.5
Over 36 months .....	47	120	84	33.3

TABLE IV.—Average systolic blood-pressures and pulse rates for 404 men of the 1910-Group, arranged by length of Philippine residence. (12.5-centimeter armlet.)

Length of tropical residence.	Number of men.	Average pressure.	Average pulse.	Average age.
		<i>mm.</i>		
3 months or less .....	158	116	77	27.0
3 to 6 months.....	74	120	80	27.0
6 to 9 months.....	88	117	75	27.2
9 to 12 months.....	59	113	73	30.3
Over 12 months .....	25	124	77	33.3

TABLE V.—Average systolic blood-pressures and pulse rates for 991 men, the combined 1909-Group and 1910-Group, arranged by length of Philippine residence. (12.5-centimeter armlet.)

Length of tropical residence.	Number of men.	Average pressure.	Average pulse.	Average age.
		<i>mm.</i>		
3 months or less .....	284	114	76	23.2
3 to 6 months.....	88	120	80	26.9
6 to 9 months.....	211	114	76	25.7
9 to 12 months.....	291	117	85	25.7
Over 12 months .....	167	120	80	29.9

It will be observed that in all 3 tables the blood-pressure is lower during the first three months of tropical residence than at any subsequent time, with two exceptions. The variations between the average readings for the different quarterly periods are slight, rarely exceeding 6 millimeters, and there seems to be no consistent rise or fall of pressure with increasing length of tropical service. The fact that the last readings in Tables IV and V and the last 3 in Table III are rather higher than the earlier ones can best be explained by consulting the column of ages, when it will be seen that the average age of the men for these periods was considerably higher than for those who had served shorter terms in the Philippines. The reason of this is that most of the individuals who stay longer than two years in the Archipelago are old soldiers, desirous of taking advantage of the fact that Philippine duty counts as double time in reckoning the thirty years of service necessary for retirement. Pulse rates in all the 3 tables are somewhat elevated above the average for the temperate zone, but there is no indication that increasing length of service aggravates the tendency to undue rapidity of heart action.

Tables VII and VIII show that during a period of one year, throughout which observations were made quarterly, there was no progressive alteration in blood tension and that the pressure was not materially different at the beginning and at the end of this year of observation.

Musgrave and Sison<sup>(6)</sup>, working in Manila and using the Erlanger instrument with a 12.5-centimeter armlet, found among 97 foreigners, mostly Americans from the Civil Service and the United States Army, that the blood-pressures were as shown in Table VI.

TABLE VI.—Average systolic blood-pressures of 97 foreigners in Manila, according to Musgrave and Sison. (12.5-centimeter armlet.)

Length of residence.	Pressure.
<i>Years.</i>	<i>mm.</i>
1 or less.	124
1 to 5	115
5 to 10	116
Over 10	113

It will be observed that Musgrave and Sison did not obtain readings during the first twelve months which were as low as ours. Their figures after one year of tropical residence coincide with what we found during the first year. In their article these observers conclude that blood-pressure in the Tropics is materially reduced. In view of the standards for temperate climates recognized by Janeway,(3) Gallavardin,(4) Woley,(5) and Bachmann(7) it seems to us that the average pressure of 124 millimeters found by Musgrave and Sison (with a 12.5-centimeter armlet) is not low and that even the average of 115 millimeters could not be considered so low as to be of much significance.

#### SUMMARY OF INFLUENCE OF THE PHILIPPINE CLIMATE.

Reduced to the basis of a 12.5-centimeter armlet we found the average blood-pressure for healthy white men in the Philippines to be 115 millimeters for those between 15 and 30 years of age and 118 millimeters for those from 30 to 40 years old. These figures are little if any below those to be expected in a temperate climate when a 12.5-centimeter cuff is employed. The lowest readings were obtained in the first three months of Philippine service. There was no progressive tendency for the pressure to increase or to decrease with continued tropical residence up to a little over three years, beyond which point our observations do not extend. The pulse rate was constantly increased, averaging 9 beats above the usual standard of 72 per minute.

#### INFLUENCE OF SEASON ON THE BLOOD-PRESSURE AND PULSE RATE.

The hottest part of the year in the regions where our observations were made is in the second quarter, April, May, and June. The rains usually begin in June or July and last till October or November. December, January, and February are comparatively cool with a mean temperature of about 25° C. (77° F.). Tables VII and VIII have been prepared to show the influence of season on the blood-pressure and pulse rate. It should be noted that in the 1909-Group the observations began in the first quarter of the calendar year whereas in the 1910-Group they commenced in the second quarter. The individual observations could not of course all be made on the same date. In fact they are spread over a period of about six weeks, but the majority were made in the middle month of the designated quarter.

TABLE VII.—Average systolic blood-pressure and pulse rates for 587 men of the 1909-Group, the 4 observations on each man being arranged by season. (12.5-centimeter armlet.)

Observation.	First quarter 1909.	Second quarter 1909.	Third quarter 1909.	Fourth quarter 1909.
Blood-pressure ..... millimeters.	116	111	114	116
Pulse rate .....	82	88	87	83

TABLE VIII.—Average systolic blood-pressures and pulse rates for 404 men of the 1910-Group, the 5 observations on each man being arranged by season. (12.5-centimeter armlet.)

Observation.	Second quarter 1910.	Third quarter 1910.	Fourth quarter 1910.	First quarter 1911.	Second quarter 1911.
Blood-pressure ..... millimeters.	117	118	118	118	118
Pulse rate .....	77	77	78	77	77

In the 1909-Group it will be seen that there was a drop in pressure of 5 millimeters in the second quarter and of 2 millimeters in the third quarter of the calendar year. The months during which the marked reduction of 5 millimeters occurred are the hottest of the year. In the 1910-Group there was a decrease of 1 millimeter in the second quarter, 1910. If the two groups were combined the mean drop in the second quarter would be about 3 millimeters. It appears, therefore, that there is a slight but probably unimportant alteration in blood-pressure in the Philippines as a result of the seasonal changes. The pulse rate was unaltered throughout the year in the 1910-Group, but showed an increased rapidity of 5 or 6 beats per minute during the hottest period in the 1909-Group.

#### INFLUENCE OF AGE ON BLOOD-PRESSURE AND PULSE RATE.

It will be seen on consulting Table II that there was a fairly well marked tendency for the blood-pressure to increase with age, the average for the period 18 to 20 years being 115.0 while that for the period 35 to 40 years was 120.5. The subgroup over 40 years of age contained no man over 50 and the average age for the group was only 43.3 years, which probably accounts for the fact that higher readings were not encountered in this subgroup. Increasing age produced no constant alteration in the pulse rate.

These changes in pressure with advancing years correspond with the experience of observers in the temperate climates. The degree of increase found in our series for men below 40 years of age was rather less marked than that found by Woley in Chicago and Bachmann in Philadelphia. Our number of men over 40 years old is too small to be of value in giving average results.

#### INFLUENCE OF COMPLEXION ON BLOOD-PRESSURE AND PULSE RATE.

As stated in the introduction we have been carrying out a series of observations to determine if blonds were more susceptible than brunettes to the influence of the Tropics. Pulse and blood-pressure observations formed a part of this work and the results are shown in Tables IX and X.

TABLE IX.—Comparative average systolic blood-pressures and pulse rates for 111 blonds and 118 brunettes, 1909-Group. (12.5-centimeter armlet.)

Type.	Average age.	First quarter 1909.		Second quarter 1909.		Third quarter 1909.		Fourth quarter 1909.		Average for year.	
		Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.
	Years.	mm.		mm.		mm.		mm.		mm.	
Blond.....	25.5	116	82	113	93	114	89	117	85	114.8	87.2
Brunette.....	25.1	119	86	115	92	115	94	118	86	116.8	89.2

TABLE X.—Comparative average systolic blood-pressures and pulse rates for 206 blonds and 198 brunettes, 1910-Group. (12.5-centimeter armlet.)

Type.	Average age.	Second quarter 1910.		Third quarter 1910.		Fourth quarter 1910.		First quarter 1911.		Second quarter 1911.		Average for year.	
		Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.	Pres-sure.	Pulse.
	Years.	mm.		mm.		mm.		mm.		mm.		mm.	
Blond.....	27.4	116	77	119	78	118	78	117	77	118	77	117.6	77.3
Brunette....	28.1	118	78	117	77	118	78	118	77	117	77	117.6	77.3

It will be observed that the average pressures throughout the year for the blonds and brunettes of the 1910-Group are identical while in the smaller 1909-Group the difference is only 2 millimeters of mercury. If the two groups are combined we obtain an average for 317 blonds of 116.7 millimeters and for 316 brunettes of 117.3 millimeters a difference of only 0.6 millimeter. The pulse rate for the two complexion types is the same in the 1910-Group and varies only 2 beats in the 1909-Group. Therefore it can be concluded that the complexion type does not appreciably affect the blood-pressure or the pulse rate in the Tropics when men are at rest. To determine if there was a difference after exercise we had special observations on the pulse and blood-pressure taken on two occasions, once near the beginning and once near the end of the year of observation. The results appear in Table XI.

TABLE XI.—Comparative average systolic blood-pressures and pulse rates on 136 blonds and 124 brunettes of the 1910-Group after exercise. (12.5-centimeter armlet.)

Type.	Second quarter 1910.		Second quarter 1911.		Average for two observations.	
	Pressure.	Pulse.	Pressure.	Pulse.	Pressure.	Pulse.
	mm.		mm.		mm.	
Blond.....	125.4	85.9	123.8	82.7	124.6	84.3
Brunette.....	128.2	87.4	125.7	83.8	127.0	85.6

These observations were made as soon as possible after the men had completed a march, a period of drill, or some other form of exercise

carried on out of doors. The exercise was as far as practicable the same for the two complexion types. On comparing the table with the preceding one, which deals with the same men when at rest, it is clear that the result of exercise was to raise the blood-pressure by an average of from 7 to 9 millimeters, and the pulse rate by an average of 7 beats. This is what would be expected in the case of healthy well-trained men engaged in moderate out-door work. When we come to compare the two complexion types it will be seen that both pulse rate and blood-pressure are slightly higher for the brunettes. However, the average differences are so small that they are probably of no importance, and it is our opinion that variation in complexion does not produce any significant change in the blood-pressure and pulse rate either at rest or during exercise.

INFLUENCE ON THE BLOOD-PRESSURE AND THE PULSE RATE OF THE USE OF ORANGE-RED UNDERWEAR AND HAT LININGS.

Table XII was prepared as a part of the data which went to show that orange-red under-garments and hat linings for use in tropical countries were of no value.

TABLE XII.—Comparative average systolic blood-pressures and pulse rates for 294 men wearing orange-red garments and 294 men wearing white ones, 1909-Group. (12.5-centimeter armlet.)

Clothing.	Average age.	First quarter 1909.		Second quarter 1909.		Third quarter 1909.		Fourth quarter 1909.		Average for year.	
		Pressure.	Pulse.	Pressure.	Pulse.	Pressure.	Pulse.	Pressure.	Pulse.	Pressure.	Pulse.
	Years.	mm.		mm.		mm.		mm.		mm.	
Orange-red -----	25.4	115	82	111	88	112	88	115	83	113.6	85.1
White -----	25.4	117	82	112	89	115	87	117	83	115.0	85.2

Exposure to ultra-violet rays is said to lower blood-pressure and some have considered the sunlight in the Tropics to be richer in these rays than it is in temperate regions. If such be the case it is conceivable that the protection of the greater part of the body with a color which intercepts the actinic rays of the solar spectrum might have some effect on the blood-pressure. The experiment showed a lower blood-pressure for those wearing the orange-red garments, but the difference is so slight that, in our opinion, it should be attributed to chance rather than to the influence of the clothing. At the different quarterly periods the pressure of the orange-red group ranged from 1 to 3 millimeters lower, and for the entire year the average for the orange-red group was 1.4 millimeters lower than for the white. Such slight differences are of no significance. The averages for the pulse rate throughout the year varied by only 0.1 of a beat.

INFLUENCE OF INDIVIDUAL SIZE OF THE MEN ON THE BLOOD-PRESSURE  
AND PULSE RATE.

Since the heights and weights of all of the soldiers in our series were on record it seemed an excellent opportunity to investigate the influence of individual size on blood-pressure, a phase of the subject in regard to which few data are available. In addition to the 992 soldiers for each of whom we had an average pressure, deduced from 4 or 5 readings taken at intervals during a year, there were a number of other men for whom 1, 2, or 3 pressure readings had been taken and the observation then discontinued for one reason or another. The individual averages for these men have been combined with the averages for the 992 previously considered, making a total of 1,243 men on whom 5,775 blood-pressure readings had been made. These men were then divided into groups according to height in inches. The results are shown in Table XIII.

TABLE XIII.—Average systolic blood-pressure and pulse rates, based on 5,775 observations of each made on 1,243 healthy soldiers in the Philippines, arranged according to height. (12.5-centimeter armlet.)

Range of height.	Average weight.			Number of men.	Average pressure.	Average pulse.	Average age.	Average tropical service.
	<i>Cm.</i>	<i>Lbs.</i>	<i>Kgms.</i>		<i>mm.</i>		<i>Years.</i>	<i>Months.</i>
Under 64 inches -----	162.5	132.9	60.4	27	117.9	79.0	27.6	13.4
64 inches <sup>a</sup> -----	162.5	134.7	61.2	114	114.7	80.3	26.7	17.1
65 inches -----	165.0	139.9	63.6	157	116.0	80.0	26.0	15.9
66 inches -----	167.6	141.9	64.5	187	115.5	81.5	27.2	17.2
67 inches -----	170.1	144.4	65.6	225	116.2	80.4	26.7	16.8
68 inches -----	172.7	147.2	66.9	251	115.7	82.3	26.4	17.8
69 inches -----	175.2	152.7	69.4	127	116.2	82.6	26.2	16.1
70 inches -----	177.7	155.6	70.7	80	117.9	80.2	27.1	16.0
71 inches -----	180.3	159.0	72.3	40	119.3	81.5	26.6	15.2
72 inches and over -----	182.8	164.5	74.8	35	120.6	83.0	25.8	17.6
Averages -----		145.5	66.1		116.2	81.2		

<sup>a</sup> This means that the men in the group were 64 inches or more, but less than 65. The next figure means that they were 65 or more, but less than 66. The same explanation applies to the subsequent figures.

It is to be observed in Table XIII that the weight progressively increased with the height and that the average age and the average length of tropical service did not vary materially in any of the height groups. Therefore any difference in blood-pressure observed may safely be attributed to the influence of height and weight. It is plain that there is no progressive rise of blood-pressure with increasing size up to and including 70 inches (177.7 centimeters) in height. For the groups 71 inches (180.3 centimeters) and over 72 inches (182.8 centimeters) there does appear a tendency for the blood-pressure to rise 2 or 3



millimeters, but these groups are relatively small so that the slight increase in pressure may have been due to chance. On the whole it can be said that there is no clearly marked tendency for either pulse or blood-pressure to rise with increasing height and weight of the individual.

INFLUENCE OF RACE ON BLOOD-PRESSURE AND PULSE RATE IN  
THE TROPICS.

In order to determine the blood-pressure of healthy adult Filipino males 552 observations were made on 386 Filipinos. Several tribes were represented such as Tagalogs, Ilocanos, Macabebes, and Visayans, but they did not differ essentially in physique, habits, or character of residence. Two hundred were soldiers and the remainder servants, laborers, and convicts. Most of the observations were made by the Board, but a part were by the officers referred to in footnote 3. The majority of these observations were taken with an 8-centimeter armlet. For the observations on 120 Filipinos the pressures were taken with both a 12.5-centimeter and an 8-centimeter armlet, and it was found that the latter registered 6 millimeters higher than the former. This amount has accordingly been deducted from the average of the readings made with the 8-centimeter cuff.

The average blood-pressure, on a basis of a 12.5-centimeter armlet, for 100 soldiers of the Philippine Scouts was 115.0 millimeters and for 100 soldiers of the Philippines Constabulary was 115.9 millimeters. In both groups the ages ranged from 15 to 40 and the average age was 24.7 years for the Scouts and 25.2 years for the Constabulary. For 145 Filipinos from various sources, ranging from 15 to 40 years of age and averaging 24.1 years, the average pressure was 115.7 millimeters. When using the *actual* 12.5-centimeter armlet the average of 166 readings on 120 Filipinos, ranging in age from 15 to 40 years, was 116.7 millimeters. *We may therefore conclude that the mean blood-pressure for Filipinos during the period of 15 to 40 years of age (average about 25 years) is 115 or 116 millimeters and that it does not differ from the pressure at the same ages for Americans residing in the Philippines. For neither race is it very materially below the figures to be expected for white men residing in temperate climates.*

Musgrave and Sison<sup>(6)</sup> obtained decidedly lower pressures in a series of 49 Filipinos, for whom the age limits are not stated. These observers found an average of 108 millimeters for 30 males and 113 for 19 females. We do not think that any general deductions should be drawn from such a small series. It is very likely that chance may have been an important factor in producing these low readings, especially in view of the fact that the usual relationship of pressures for the two sexes was reversed, the females having the higher tension, whereas the general experience elsewhere is that women show a systolic pressure lower by about 10 millimeters.<sup>(3)</sup>

Two small groups among our Filipinos, which are not included in the above consideration, are of interest. One is a group of 26 Filipinos ranging in age from 40 to 75 years, the average being 50.6 years. The mean pressure was 144.8. This seems a high figure, considering the average age, and possibly may signify that the elevation from increasing years comes on earlier for Filipinos than for white men. Casual observation suggests that the other indications of senility occur early among tropical natives. The other group consists of 20 Igorots, all apparently young, but whose exact ages could not be determined. They gave an average of 122.0 millimeters. The Igorots were living at an altitude of 1,500 meters in a comparatively temperate climate, and though smaller in stature are better developed physically than the lowland natives. Their blood-pressures averaged 6 or 7 millimeters higher than the mean for the lowland Filipinos, the increase probably being due to the altitude.<sup>(8)</sup> The whole Filipino group, except the Igorots, is arranged by ages in Table XIV.

TABLE XIV.—Average systolic blood-pressures for 366 lowland Filipinos; arranged by ages. (12.5-centimeter armlet.)

Age period.	Number of men showing pressures from—									Total number of men.	Average pressures.
	80 to 90 mm.	91 to 100 mm.	101 to 110 mm.	111 to 120 mm.	121 to 130 mm.	131 to 140 mm.	141 to 150 mm.	151 to 160 mm.	161 to 200 mm.		
15 to 20 years		4	11	18	6	1				40	mm. 112.8
20 to 25 years	1	10	49	59	28	8	3	2	1	161	115.4
25 to 30 years		7	21	32	23	9	2	1		95	117.0
30 to 35 years	1	2	6	5	10	3	1			28	116.9
35 to 40 years	1	1	5	5	3	1				16	112.3
Over 40 years			4	4	1	4	1	6	6	26	144.8
Total	3	24	96	123	71	26	7	9	7	366	

It will be seen that the blood-pressure showed a tendency toward progressive increase with age except in the period 35 to 40 years. The records for this period contained 5 exceptionally low blood-pressure readings and as there were in all only 16 men in this subgroup it is probable that such a low reading for the ages of 35 to 40 is merely the result of accident and would not be manifest in a larger series. Pulse rates were recorded only for the Scout and Constabulary groups and averaged for the former 75.7 (blood-pressure 115.0 millimeters) and for the latter 82.5 (blood-pressure 115.9 millimeters). These averages do not vary materially from the pulse rates found for our various groups of American soldiers in the Philippines.

## CONCLUSIONS.

1. The mean blood-pressure in temperate climates for healthy males between 15 and 30 years of age lies between 115 and 122 millimeters of mercury when a 12.5-centimeter armlet is employed.

2. When the 12.5-centimeter armlet is used the blood-pressure of American soldiers serving in the Philippines averages 115 millimeters for the period 18 to 30 years of age, and 118 for the period 30 to 40 years.

3. This indicates that the blood-pressure of Americans residing in the Philippines differs but little if any from the average at home.

4. Usually the lowest readings for Americans living in the Philippines were obtained in the first three months of tropical residence, but there was no progressive tendency for the pressure average to rise or to fall with increased length of residence up to a limit of three years, beyond which our work did not extend.

5. The blood-pressure of Americans was lower during the hottest part of the year, but the difference was very slight, only about 3 millimeters.

6. There was a well marked tendency for the blood-pressure of Americans to rise with increasing age.

7. Neither complexion type nor the use of underwear and hat linings of orange-red color exerted any appreciable influence on the blood-pressure of American soldiers.

8. There was no well marked tendency for the blood-pressure or pulse rate to rise with increasing height and weight of the individual.

9. As was to be expected, exercise raised both the blood-pressure and the pulse rate.

10. Using a 12.5-centimeter armlet the average blood-pressure of Filipinos was found to be 116 millimeters for a large group of males ranging from 15 to 40 years of age and averaging 25 years. This pressure was practically identical with that for the group of white men of the same average age and living in the Philippines.

11. There is a well marked tendency for the blood-pressure of Filipinos to rise with increasing age.

12. The pulse rate of active Filipinos and Americans living in the Philippines averages a few beats above the usual standard of 72 per minute.

In closing we wish to express our obligations to the medical officers mentioned in footnote 3, who by their earnest and continued efforts made possible the collection of the statistics on which this report is based.

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# THE RED BLOOD CORPUSCLES AND THE HÆMOGLOBIN OF HEALTHY ADULT AMERICAN MALES RESIDING IN THE PHILIPPINES.

BASED ON 1,418 RED CELL COUNTS AND 1,433 HÆMOGLOBIN ESTIMATIONS  
PERFORMED ON 702 SOLDIERS.<sup>1</sup>

By WESTON P. CHAMBERLAIN.<sup>2</sup>

(From the United States Army Board for the Study of Tropical Diseases.)

The expression "tropical anæmia" is one that often occurred in the older treatises on diseases of hot countries, but more recent investigations have shown that most of the conditions formerly so designated are in reality instances of secondary anæmia due to infections with various parasites, notably plasmodia and uncinaria.

Scheube says "there is no anæmia caused by the tropical climate alone."<sup>(1)</sup> The investigations of Marettang, van der Scheer, Eijkman, Glongner and F. Plehn<sup>(1)</sup> on white men living in the Tropics showed no material deviations from the normal condition as observed in Europe. Castellani and Chalmers<sup>(2)</sup> state that a certain number of Europeans in the Tropics take on "a peculiar whitish color, even in cases in which the blood examination does not reveal any sensible decrease in the amount of hæmoglobin." Eijkman<sup>(1)</sup> also refers to this phenomenon. Lehmann and van der Scheer<sup>(1)</sup> and Musgrave and Sison<sup>(3)</sup> consider this pallor of the skin to be a local vaso-motor condition.

In 1908 Wickline<sup>(4)</sup> reported the result of examinations of the blood of American soldiers in the Philippines. The men arrived in the Archipelago in June, 1905, and the first observations were made in September of the same year. His results, which are given in Table I, showed that there was a progressive fall in the percentage of hæmoglobin and a regular rise in the number of erythrocytes except at the last observation period. The color index progressively decreased.

TABLE I. Wickline's average estimations of the erythrocytes and hæmoglobin of American officers and soldiers who arrived in the Philippines in June, 1905.

Number of men examined.	Dates of examination.	Average number of erythrocytes per cubic millimeter.	Average hæmoglobin.	Average color index.
			<i>Per cent.</i>	
70	Sept., 1905	4,980,555	94	0.94
104	Dec., 1905	5,343,595	89	0.83
97	Aug., 1906	5,429,960	86	0.79
81	Apr., 1907	5,330,888	83	0.78

<sup>1</sup> Published with permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> Weston P. Chamberlain, major, Medical Corps, United States Army, president of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

During the last three years the United States Army Board for the Study of Tropical Diseases has been carrying out two series of observations, one to determine if any benefit resulted from the use of orange-red underwear in the Philippines,<sup>(5)</sup> and the other to decide if complexion type was a factor in the resistance of white men to tropical influences.<sup>(6)</sup> During this work a large number of observations on the blood were made by the members of the Board and by certain medical officers of the Army who were detailed to make the examinations under the supervision of the Board.<sup>3</sup> The large number of independent observers minimizes as far as possible the influence of the personal equation in this work. The red cells were counted with the Thoma-Zeiss hæmocytometer. The hæmoglobin estimations were made in most cases with Dare's hæmoglobinometer and in the remainder with the von Fleischl instrument. The number of men observed is so large that the element of chance is eliminated. With one exception the stations where the soldiers resided were close to the coast line. Most of them were near sea-level and of the posts which were not so situated none were at an altitude exceeding 600 feet (200 meters). It should be understood that all of the men were healthy soldiers performing their full military duty. The results are shown in Tables II and III. The average age of the men in Table II was 25.3 years and of those in Table III was 27.7 years.

TABLE II.—Average erythrocyte counts and hæmoglobin estimations on 65 American soldiers who at the date of the first examination had served on the average 14.9 months in the Philippines.

Dates of examinations.	Average number of erythrocytes per cubic millimeter.	Average hæmoglobin.	Average color index.
		<i>Per cent.</i>	
January, 1909.....	5,276,000	89.3	0.85
July, 1909.....	5,355,000	88.2	0.82
December, 1909.....	5,152,000	90.0	0.87

\*The medical officers who were engaged in making the blood examinations referred to in this sentence were the following: Majors A. E. Truby and Roger Brooke, jr.; Captains E. G. Bingham, J. R. Barber, Mahlon Ashford, E. G. Huber, H. M. Snyder, and W. L. Hart; 1st Lieutenants J. B. H. Waring, W. R. Dear, C. E. Doerr, F. S. Wright, C. G. Snow, N. L. McDiarmid, Armin Mueller, T. J. Leary, M. C. Stayer, L. C. Garcia, and C. E. Fronk, Medical Corps; and 1st Lieutenants W. F. de Niedman, and C. A. Betts, Medical Reserve Corps.

TABLE III.—Average erythrocyte counts and hæmoglobin estimations on 601 American soldiers who at the date of the first examination had served on the average 6.6 months in the Philippines.

Dates of examinations.	Average number of erythrocytes per cubic millimeter.	Average hæmoglobin.	Average color index.
		Per cent.	
May and June, 1910 -----	5,111,000	90.3	0.88
May and June, 1911 -----	5,206,000	89.6	0.86

It will be seen that in character our blood examinations agree with those of Wickline, although the alteration which he found with increasing length of tropical residence are not as pronounced in our series as in his. Our average erythrocyte counts at different periods range from 5,111,000 to 5,355,000, and the average hæmoglobin readings from 88 to 90 per cent. The color index is consequently considerably below unity, varying from 0.82 to 0.88.

In Tables IV and V is shown the range covered by the individual red counts and hæmoglobin estimations for a body of healthy American soldiers, who at the date of examination had served in the Philippines for an average of twenty months, the length of this service being for no man less than fourteen months. These tables include all the examinations that are shown in the last column of averages in Tables II and III, together with a few others which were not entered in Tables II and III because there were no preliminary examinations for the individuals concerned.

TABLE IV.—Range of erythrocyte counts for 687 healthy American soldiers who at date of count had served on the average twenty months in the Philippines.

Range of erythrocyte count per cubic millimeter.	Number of men.	Per cent of total number.	Range of erythrocyte count per cubic millimeter.	Number of men.	Per cent of total number.
Under 4,000,000 -----	15	2.2	5,500,000 to 5,749,000 -----	76	11.1
4,000,000 to 4,249,000 -----	26	3.8	5,750,000 to 5,999,000 -----	39	5.6
4,250,000 to 4,499,000 -----	37	5.4	6,000,000 to 6,224,000 -----	35	5.1
4,500,000 to 4,749,000 -----	60	8.8	6,225,000 to 6,499,000 -----	24	3.5
4,750,000 to 4,999,000 -----	112	16.3	6,500,000 to 6,749,000 -----	12	1.7
5,000,000 to 5,224,000 -----	155	22.5	6,750,000 to 6,999,000 -----	14	2.1
5,225,000 to 5,499,000 -----	77	11.2	Over 7,000,000 -----	5	0.7

TABLE V.—*Range of hæmoglobin readings for 702 healthy American soldiers who at date of examination had served on the average twenty months in the Philippines.*

Range of hæmoglobin.	Number of men.	Per cent of total number.	Range of hæmoglobin.	Number of men.	Per cent of total number.
Under 80 per cent.....	8	1.1	90 to 94 per cent.....	261	37.2
80 to 84 per cent.....	64	9.2	95 to 99 per cent.....	136	19.4
85 to 89 per cent.....	185	26.4	100 per cent or over.....	48	6.7

It will be noted in the erythrocyte counts that there was a considerable excursion below and a still greater excursion above the 5,000,000 mark. The men with cell counts between 5,000,000 and 6,000,000 per cubic millimeter constituted 50.4 per cent of the total 687, while those with counts above 6,000,000 formed 13.1 per cent. The table of hæmoglobin estimations shows that 89.7 per cent of the men gave readings of 85 per cent or upward.

The normal erythrocyte count of young adult males at sea-level in temperate climates may vary considerably from the conventional 5,000,000 per cubic millimeter. Cabot states that 6,000,000 is by no means rare among healthy young men and that higher figures are seen occasionally. Among 50 young medical students in the United States Hewes(7) found an average of 5,809,000; the lowest being 5,120,000. Sorensen (11) found an average of 5,606,000 for male students ranging from 19.5 to 22 years of age and of 5,340,000 for young physicians from 25 to 30 years old. Ewing,(8) speaking of Welcker's estimate of the normal red cell count as 5,000,000 for men and 4,500,000 for women, says:

"Perhaps the chief contribution of later observers using Thoma's instrument has been the proof that the numbers are more apt to exceed rather than fall below these averages, especially in men, a fact that has become more certain from the more careful estimates of the last decade. Thus the average obtained by Helling was 5,910,000; by Frederickson, 5,072,000; Zaslein, 5,010,000; Neubert, 5,603,000; Graber, 5,081,000; Stierlin, 5,752,000; Reinicke, 5,209,667; Andriezen, 6,000,000; Hayem 5,500,000."

In view of the above averages it will be seen that the erythrocyte counts obtained by Wickline and by ourselves among healthy young soldiers in the Philippines could not be considered as differing from the normal as seen in Europe and America.

For 70 healthy American soldiers stationed in New Orleans, and in whom uncinariasis had been ruled out by repeated examinations of the stools, we found an average of 94.2 per cent of hæmoglobin.(12) The von Fleischl instrument was used and the average age of the men was about 28 years. Our own experience elsewhere in the United States has been that readings with this instrument rarely reach 100 per cent.

Faught(10) considers 90 or 95 per cent with the von Fleischl apparatus to be normal. The relative percentage of hæmoglobin as estimated by clinical hæmoglo-



binometers, is figured by Stierlin(9) to be 88.8 for the ages 18 to 25 years and 100.0 for the ages 25 to 45 years. Since the average age of the groups of men we examined was 25.3 years for that considered in Table II and 27.7 years for that in Table III, it will be seen that the hæmoglobin percentages, which ranged from 88 to 90, were probably a little below the standard to be expected in the temperate zone. In the case of Wickline's series the reduction of hæmoglobin was more marked, but even among his men it was not low enough to indicate a definite state of chlorosis or anæmia.

The color index, or hæmoglobin quotient, indicating the richness in hæmoglobin of the individual red cells, is set by most authors at a normal of 1, this figure being based on an average erythrocyte count of 5,000,000 and an average hæmoglobin estimation of 100 per cent. Bearing in mind the evidence adduced in the above paragraphs, namely that the red cell counts of young men range above 5,000,000 and that the hæmoglobin reading commonly does not reach as high as 100 per cent, it becomes obvious that color indices as great as unity are not to be expected in most instances. However, we have not been able to find in Manila any statistics showing the mean index for healthy and vigorous young adults in the United States or Europe. It seems probable that average hæmoglobin quotients between 0.82 and 0.88 such as were found in our examinations, may be a little low, but not sufficiently so to be considered as definite indications of anæmia or chlorosis. We feel sure that such reduction in the hæmoglobin quotient as did occur among the men considered in Table III is not due to a prevalence of mild uncinariasis, since the stools of these men were examined at the conclusion of the observation period and only 2.3 per cent were found to contain hookworm eggs.

As regards the influence on the blood of the use of garments designed to absorb the actinic rays of the sun, it was shown in a former report of the Board(5) that the number of erythrocytes and the percentage of hæmoglobin were constantly a little higher for the men wearing orange-red underclothing than for those wearing white. This difference was thought to be due to concentration of the blood in those persons wearing the orange-red underwear, which was warmer than the white and therefore caused more profuse perspiration. As regards complexion type another report of the Board(6) showed that there was no constant or appreciable difference between the red cell counts and the hæmoglobin estimations of blond and brunette American soldiers who had served continuously in the Philippines for periods ranging from eighteen to twenty-four months.

In closing we wish to express our obligations to the medical officers referred to in footnote 3, who assisted the Board in making the hæmatologic examinations on which this report is based.

## CONCLUSIONS.

From our own work it may be concluded that, after about twenty months of Philippine service, healthy American soldiers, living near sea-level and averaging 26 years of age, will show:

1. A red cell count averaging 5,200,000 per cubic millimeter, and rarely falling below 4,500,000.

2. A hæmoglobin reading averaging 89.6 per cent, and rarely falling below 85 per cent.

3. A color index averaging 0.86 or 0.87.

Such a red cell count does not differ from the normal at present recognized for healthy young men in the temperate zone. The hæmoglobin percentage and the color index are probably a little low, but not sufficiently so to indicate a definite anæmia. The pallor not infrequently met with among apparently healthy persons in the Tropics we believe to be due as a rule to superficial ischæmia and not to a deficiency in the total quantity, or in any particular constituent, of the blood.

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THE OCCURRENCE IN THE PHILIPPINES OF ASSOCIATED  
SPIROCHÆTÆ AND FUSIFORM BACILLI IN ULCERS OF  
THE THROAT (VINCENT'S ANGINA), OF THE MOUTH,  
AND OF THE SKIN, AND IN LESIONS OF THE  
LUNGS (BRONCHIAL SPIROCHÆTOSIS).<sup>1</sup>

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By WESTON P. CHAMBERLAIN.<sup>2</sup>

(*From the United States Army Board for the Study of Tropical Diseases.*)

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In our quarterly report of March 31, 1910,<sup>(1)</sup> we referred briefly to the finding of several cases of the so-called Vincent's angina in the Philippines, and subsequently Bloombergh,<sup>(2)</sup> then a member of the Board, reported more fully on the subject. Since that time we have been on the lookout for the presence of Vincent's symbiotic organisms in all throat lesions coming to the notice of the Board and a large number of cases have been detected.

In 1894 Plaut<sup>(3)</sup> and in 1896 Vincent<sup>(4)</sup> called attention to a fusiform bacillus, commonly associated with a spirillum, in ulcerative lesions of the throat, pharynx, and mouth. Since that time many writers have confirmed these observations and the two organisms have been found in various other kinds of lesions. Weaver and Tunnicliff<sup>(5)</sup> have demonstrated the organism in noma and others have found them in ulcerative stomatitis, diphtheria, carious teeth, hospital gangrene, appendicitis, brain abscess, fœtid bronchitis, pyorrhœa alveolaris, and syphilitic lesions. Vincent,<sup>(10)</sup> Smith and Peil,<sup>(10)</sup> Bruce,<sup>(7)</sup> and ourselves<sup>(8)</sup> have met with similar forms in ulcerations of the skin. Recently Peters in Cincinnati has reported a case of fatal lobar pneumonia, a case of fœtid bronchitis and a case of septic infection of the hand, in all 3 of which fusiform bacilli and spirochætæ were present in large numbers in the exudate. In the case of hand infection the affected member had been injured by the teeth of another person. Hultgen<sup>(12)</sup> reports a similar case of hand infection where the patient had the nail-biting habit and the same organisms were found about the teeth.

*Bacillus fusiformis* of Plaut and Vincent is about 10  $\mu$  in length, the limits of size generally being set at 3 and 15  $\mu$ . Occasionally much larger ones have been seen by us. From the center the bacillus tapers toward the ends which are

<sup>1</sup> Published with permission of the Chief Surgeon, Philippines Division.

<sup>2</sup> Weston P. Chamberlain, major, Medical Corps, United States Army, president of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

sometimes blunt and at other times sharp. The organisms may be straight or slightly curved and are frequently arranged in pairs, end to end. Occasionally wavy forms are seen. They stain readily with carbol-fuchsin, Loeffler's methylene-blue, or Giemsa's stain, and many show irregularity in the intensity of the staining which gives them a quite characteristic banded appearance. They are non-motile.

The spirilla or spirochætæ are longer than the bacilli, ranging from 15 to 50  $\mu$  in length, and are made up of a variable number of undulations, usually from 3 to 5. They are usually very slender and in fresh preparations are extremely active. With the ordinary aniline dyes they stain less intensely than do the fusiform bacilli and occasionally present a beaded appearance as is shown in one of the appended photomicrographs.

Although several attempts have been made to cultivate these organisms from lesions containing them in great numbers we have been uniformly unsuccessful. They have been grown in pure culture by Weaver and Tunnicliff (5) (9) on slants of ascitic agar (1-3) and by Peters on Dorset's egg medium, in both cases under anaerobic conditions. Tunnicliff and some others consider that the fusiform bacillus and the spirochætæ are different forms of one organism. Some observers consider them to be protozoa.

In smears from oral and faucial ulcers the symbiotic organisms of Vincent's angina are usually associated with varying numbers of other bacteria, such as staphylococci, streptococci, and different species of bacilli, including the Klebs-Loeffler bacillus. Abel has found the organisms in normal mouths, and Gross in apparently healthy tonsils. (5) Some have suggested that to make a diagnosis of Vincent's angina the organisms should be present in preponderating numbers, as compared with other bacteria. (5) Such a distinction is unsatisfactory, but may be of some clinical use and will be to a certain extent adhered to in the following report.

#### PRESENCE OF THE ORGANISMS IN THROAT AND MOUTH LESIONS IN THE PHILIPPINES.

During the last two years we have examined all patients with throat and mouth lesions who came to our notice in Manila. There were 106 of these, and in the smears from 34 (32 per cent) the fusiform bacilli and spirochætæ of Vincent's angina were present in *preponderating numbers*. In 22 others (21 per cent) a few of these symbiotic organisms were found, so that in 53 per cent of the total 106 cases they were present to a greater or less extent. The pathologic conditions with which they were associated are shown in the following table.

TABLE I.—Occurrence of *spirochætæ* and *fusiform bacilli* in throat and mouth lesions in the Philippines.

Pathological condition.	Present in preponderating numbers.	Present in small numbers.	Absent.
Ulcers of tonsil, cause uncertain .....	16	9	8
Ulcers of tonsil, probably syphilitic .....	4	0	5
Ulcers of faucial pillars, probably syphilitic .....	0	0	3
Ulcers of gums (ulcerative stomatitis) .....	6	3	3
Ulcers of gums, probably syphilitic .....	1	0	0
Ulcer of cheek .....	0	0	1
Ulcer of soft palate, probably syphilitic .....	2	0	1
Ulcer of tongue, probably syphilitic .....	1	1	1
Membranes on tonsil, cause uncertain .....	2	4	6
Mucus patches, syphilitic .....	2	0	4
Chancre, tongue .....	0	0	1
Chancre, tonsil .....	0	0	1
Aphthous stomatitis .....	0	0	5
Diphtheria tonsilar .....	0	0	4
Tonsillitis, acute, follicular .....	3	5	6
Sprue .....	0	0	1
Carcinoma of soft palate .....	1	0	0
Total .....	<sup>a</sup> 38	22	50

<sup>a</sup> The discrepancy between 38 in this column and the 34 positive cases found is due to the fact that 4 of the cases had positive lesions in two different localities in the throat or mouth.

It will be observed that the two organisms were present in preponderating numbers in a considerable variety of conditions, the number of positive findings being highest in ulcers of the gums and of the tonsils. Twenty-seven of the lesions tabulated by us were apparently syphilitic, 2 being primary, 2 tertiary and the remainder secondary, and in these luetic cases the organisms of Vincent were found in preponderating numbers in 10 and in small numbers in 1. In not all of these presumably specific cases was the diagnosis absolutely unassailable, but in some of those in which the fusiform bacilli and spirochætæ were demonstrated in large numbers the diagnosis of syphilis was as certain as one could wish, being confirmed by the finding of *Treponema pallidum*, by the presence of a positive Wasserman reaction, or by the existence of unmistakable physical signs outside of the mouth.

Fusiform bacilli and spirochætæ were not detected in any of the 4 cases where the Klebs-Loeffler bacilli were found by cultural methods. From 44 others of the 106 cases studied, cultures on blood serum were made with negative results as far as the diphtheria bacillus was concerned. Many of these lesions showed in smears the presence of large numbers of spirochætæ and fusiform bacilli. In some of them the local appearances were strongly suggestive of diphtheritic infection.

Nearly all of our positive cases were young adult males, for the most part American soldiers. A few throat lesions among Filipinos were examined. Only one of these had any of the organisms and in this lesion they were not present in preponderating numbers.

In the patients showing fusiform bacilli and spirochætæ in preponderating numbers the clinical appearances and symptoms were so variable that no diagnosis based on them could have been of value. As shown in the table the localities affected were diverse. The ulcers were covered with white exudate in 2 and with soft grayish membranes in 8 cases. Fever was present in 6 of the cases of throat involvement, dysphagia in 16 and prostration in 1. Of the lesions on the gums 3 were very painful and 2 were painless. Most of the cases were acute, but 7 were chronic, some having had ulcers for several months.

On the assumption that carious teeth might be the cause of the frequent presence of spirochætæ and fusiform bacilli in the mouth, an examination was made of the material from the interior of the carious teeth of 10 individuals. In the smears from 3 individuals an occasional spirochæta was found, but no fusiform bacilli were seen in any instance. We also examined a number of smears from apparently normal tonsils. Most of these were negative, but in some there were a few spirochætæ and very rarely a small fusiform bacillus.

#### PRESENCE OF THE ORGANISMS IN LESIONS OF THE SKIN IN THE TROPICS.

In speaking of tropical ulcer Castellani and Chalmers say:(10) "Vincent believes the affection (*Ulcus tropicum*) to be due to the association of spirochaetes and fusiform bacilli so frequently found in such ulcers. Vincent's observations have been confirmed by Smith and Peil in Sierra Leone, Patton in Aden, and many other observers in various parts of the tropics." In 1907 Shattuck(6) working in the Philippines reported that of 34 ulcers of the skin examined by him 5 contained spirochætæ in the exudate. He states that some resembled *Spirochæta refringens* and that others appeared intermediate between that organism and *Treponema pallidum*. He concluded that the spirochætæ were not of etiologic significance because of their absence in sections. He makes no mention of having found fusiform bacilli in the smears from the ulcers, but in his photomicrographs there are some large not very clearly defined, bacilli which somewhat resemble *Bacillus fusiformis*.

Howard(13) reports spirochætæ, generally in company with *Bacillus fusiformis*, to be common in various types of ulceration in Nyasaland, and states that in sections the spirochætæ can be seen spreading into the healthy tissue in advance of other micro-organisms. He also says they may be found in nearly all foul-smelling neglected ulcers.

In January, 1911, W. J. Bruce(7) reported under the title of "Zambesi Ulcer" a condition which he had not previously seen described. The lesions, as seen by Bruce, were generally situated below the knee and consisted of punched-out ulcers which healed after one or two weeks without the production of any constitutional symptoms. In the smears from the ulcers he invariably found in great numbers a spirillum and a large fusiform bacillus.

A little time before the receipt of this report of Bruce one of us found spirochætæ and fusiform bacilli in large numbers in an ulcerated area on the foot of a Filipino. This ulcer was thought to be due to yaws, and smears from it were stained for *Treponema pertenue*. No treponemata were detected, and no other organisms except delicate spirochætæ, ranging in length from 15 to 50  $\mu$ , and heavy fusiform bacilli the length of which varied from 5 to 10  $\mu$ . Photomicrographs of the organisms are appended. We were at once impressed by the resemblance of these parasites to those described as the cause of the so-called Vincent's angina. The fusiform bacilli were of the same size and presented the same barred appearance on staining. Many were identical with *Bacillus fusiformis* of Plaut and Vincent, but on the average the ends did not seem quite as sharp as those of the organisms found in throat lesions. The spirochætæ were rather longer than those observed in the mouth and fauces and did not seem to stain as intensely with cold carbol-fuchsin. They were very slender and had from 6 to 12 shallow undulations, but differed considerably among themselves in size and shape.

Unfortunately this patient passed from observation before these organisms were demonstrated. Consequently no cultures were made and no history was obtainable.

During the last two years we have examined smears from a large number of ulcers of the skin, but have not encountered these organisms on any other occasion. Doctor R. P. Strong and others in Manila inform us that they have not met with them in lesions of the integument. Recently Lieutenant Armin Mueller, Medical Corps, United States Army, stated that he has found several such cases at Camp Jossman near Iloilo, P. I.

#### BRONCHIAL SPIROCHÆTOSIS WITH AN OCCASIONAL FUSIFORM BACILLUS.

Bronchial spirochætosis was first described by Castellani in 1906 since which date numerous cases, both acute and chronic, have been reported by observers in various tropical countries. From the description given by Castellani and Chalmers in their Manual of Tropical Medicine it appears that most, if not all, of these diagnoses, have been made from the sputum examinations alone. In 1909 Phalen and Kilbourne(11) of this Board reported a case of pulmonary spirochætosis in a Filipino, but called attention to the fact that the causative relation of the spirochætæ to the disease was not proven. The report mentions that a few large bacilli were present, but does not state whether they

resembled *Bacillus fusiformis*. Recently, on re-examining sinears from this case, we found a few perfectly typical fusiform bacilli; they had the characteristic barred appearance when stained.

In searching fresh sputa for yeast the Board recently found specimens from 2 patients which showed large numbers of actively motile spirochætæ. Both of these patients were Filipinos suffering from typhoid fever. Specimens of sputum from 32 other patients having cough with expectoration were examined and none contained spirochætæ except one which had an extremely few, thick, spiral organisms such as might easily have entered the sputum from around the necks of the teeth where such organisms are common. Of the 32 patients, 27 were Americans and 5 natives.

The histories of the 2 cases, the sputa of which contained spirochætæ, are given through the courtesy of Captains H. S. Hansell and C. L. Foster, Medical Corps, who had charge of the patients.

*Case I.*—Udasco, Private, 23rd Company Philippine Scouts, age 23. Service two years and eight months. Tribe, Ilocano. Admitted to hospital November 3, 1910. Family and previous history unknown. Bad cough for three weeks previous to admission, and slight expectoration. Noted no blood. Headache and fever but no chills. On admission to hospital patient appeared very ill. Pulse regular and normal. A few vesicles on back and chest. Râles heard over both lungs. Abdomen distended and tympanic. Liver and spleen not palpable. Subsequently spleen was found palpable. Patient ran an irregular febrile course for twenty days, followed by a period of ten days of continued high fever associated with abdominal distention and constipation (relapse?), since which time (twenty-six days) there have been several unaccountable elevations of temperature. The Widal reaction was negative November 4, 5, and 6, partial on November 7, and positive on November 8. Blood was negative for *Bacillus typhosus* on November 7. Stools and urine were only examined during convalescence when they were negative for typhoid bacilli. The condition of the patient gradually improved after the relapse, and the cough disappeared.

Eleven specimens of sputum obtained at intervals were negative for tubercle bacilli. Stools negative for amœbæ and for ova except *Tricocephalus dispar*. No malarial parasites were found. There was a slight leucocytosis ranging from 8,000 to 15,000. Differential counts showed nothing of importance, averaging; polymorphonuclears 61 per cent, small lymphocytes 36 per cent, large mononuclears 2 per cent, and eosinophiles 1 per cent. Urine during febrile period showed a trace of albumin and a few granular casts. Diazo reaction negative. Subsequently urine became normal.

On November 30 and on several succeeding days the sputum contained great numbers of spirochætæ. Prior to that no effort had been made to find them as will be explained below when referring to staining methods. The sputum was thin and watery containing a large number of small grayish flakes which consisted of masses of cocci, many kinds of bacilli, and a few epithelial cells and leucocytes. There was no blood and no bad odor.

After a lapse of over four weeks (December 31, 1910) the sputum, obtained on forced cough, was of the same flakey character as described above and contained numerous spirochætæ.



*Case II.*—Cassas, civilian employee, age 25. Tribe, Tagalog. Admitted to hospital October 31, 1910. Family history unknown. No previous illness. During last two months has had slight chills and fever at irregular intervals. Since shortly before entry had a cough with muco-purulent expectoration. Some headache, no diarrhœa. Fairly well nourished, nothing abnormal found on physical examination except fever which pursued a typical typhoid course for a period of twenty-seven days when the temperature became normal for one week since which time (three weeks) it has been subject to irregular and unaccountable elevations. The Widal reaction was partial November 1, and positive November 3. On November 1, *Bacillus typhosus* was obtained from a blood culture. On November 22 a stool culture for the same organism was positive.

This patient became very ill as his disease progressed. On November 4 he vomited a great deal. The spleen became palpable. Subsequently pulse became dicrotic and weak and tympanites developed. On November 14 complained of sore throat and a patch of exudate appeared on the left tonsil. This was negative for diphtheria and *did not show the spirochætæ and fusiform bacilli associated with Vincent's angina*. On November 17 the throat symptoms had disappeared. On November 20 patient was very weak and began to cough up bloody sputum. This bloody expectoration lasted for several days and was quite profuse. After the temperature reached normal the patient gradually improved and the cough disappeared.

In this case the blood was negative for malaria. The leucocytes ranged from 8,500 to 12,800. The differential count showed nothing of interest; polymorpho-nuclears 68 per cent, small lymphocytes 30 per cent, and large mononuclears 2 per cent. The urine during the height of the fever showed a trace of albumin and a few hyaline casts. The stools showed ova of *Tricocephalus dispar*, and *Cercomonas intestinalis*, but no amœbæ.

After the appearance of bloody sputum an examination on nine occasions was negative for tubercle bacilli and on one occasion an acid-fast bacillus shorter and thicker than the tubercle bacillus was found. This specimen was inoculated into a guinea pig and at the end of eight weeks the animal was alive and well. At autopsy it showed no indications of tuberculosis.

On one occasion motile amœbæ and a flagellate resembling a cercomonas were found in the sputum.

The character of the sputum was the same as in the preceding case except that it was blood-stained at times. It was found to contain large numbers of spirochætæ associated with many masses of bacilli and cocci. *An occasional large fusiform bacillus was seen.* The spirochætæ were found constantly present for a period of two weeks. After a lapse of nearly two weeks more (December 31, 1910), the patient meanwhile having greatly improved in condition and the blood having disappeared from the sputum, spirochætæ were still present in considerable numbers though not as numerous as at the time of the hæmorrhage. The sputum at this time, obtained only after forced coughing, was thin and watery with great numbers of the small, gray flakes described in Case I. There were no blood corpuscles.

The spirochætæ in both cases were similar in motility, shape and size, averaging about 15  $\mu$  in length. They were thin and delicate and resembled the third class described by Castellani except that none having one blunt point were noticed.<sup>(10)</sup> In one of the patients (Number II) there were found a few fusiform bacilli similar to those which are seen

in symbiosis with spirochætæ in the so-called Vincent's angina. It is interesting to note that in history, symptoms, and character of the sputum these two cases were almost identical except that one contained fusiform bacilli and the other did not. Whether the presence of a few fusiform bacilli in one of these sputa, and in the sputum formerly described by Phalen and Kilbourne, was due to a contamination of the phlegm while it was passing through the mouth can not be determined. It is certain that the bacilli were present in both sputa in much smaller relative numbers than is usually the case in ulcers of the mouth and fauces when the symbiotic bacilli and spirochætæ are encountered.

In many of the cases described in the literature spirochætosis appears to be an independent disease. In considering the two histories recorded above it must be remembered that both patients were very ill with typhoid fever and, therefore, the presence of the organisms in the bronchial secretion may have been due simply to a migration downward, in a debilitated individual, of the spirochætæ which normally have a limited habitat in the mouth. However, the persistence of the spirochætæ in the sputum far into convalescence seems to be opposed to this view of the matter.

PREVALENCE OF SPIROCHÆTÆ AND FUSIFORM BACILLI IN LESIONS  
OCCURRING IN NON-TROPICAL COUNTRIES.

These associated organisms are probably much more common in oral and faucial lesions than is generally thought to be the case and would doubtless be very frequently met with if the practice of examining smears from ulcers in those regions was more general.

Rodella found the two organisms present in about one third of the 2,000 cases of pseudo-membraneous anginas which he examined.<sup>(5)</sup> Beitzke demonstrated the organisms in 5 out of 58 patients suspected of having diphtheria. Lublowitz reports the presence of fusiform bacilli in 6 out of 38 ulcers of the mouth. Arnold found the two organisms in 3 out of 5 cases of follicular tonsilitis.

Rothwell<sup>(14)</sup> under the title of "Bronchial Vincent's Angina" reports 4 cases, which have come to his notice in Missouri, where the sputum was swarming with fusiform bacilli and spirochætæ. There was bloody expectoration and the symptoms somewhat resembled asthma. Cases of fœtid bronchitis and pneumonia have been reported in which the sputum contained these 2 organisms, but as yet the reports of pulmonary cases in temperate regions are so few that no reliable estimate can be made as to the real frequency of the condition.

It is not improbable that the organisms may go undetected more commonly than is generally supposed to be the case because of the fact that a majority of the sputa examined microscopically are stained by Gabbett's method or some similar procedure. While the spiral organisms in pulmonary spirochætosis stain well with ordinary aniline dyes, such as carbol-fuchsin or Loeffler's methylene-blue, we found that

they were not acid fast and that *they did not stain with the sulphuric-acid-methylene-blue as ordinarily used in Gabbett's method for demonstrating tubercle bacilli*. The same was found to be true for the spirochætæ in Vincent's angina. Therefore, it is evident that spirochætæ in the sputum would be likely to be overlooked in making a routine examination of the sputum for tubercle bacilli.

The occurrence of the organisms in infections of the skin in temperate regions up to the present time has been reported but rarely and no estimate can be formed as to the frequency of such lesions. The cases reported by Peters and Hultgen are referred to in the second paragraph of this article.

#### CONCLUSIONS.

From our limited series of observations it appears probable that more than one-half of the throat and mouth ulcers one is likely to encounter in the Philippines will show fusiform bacilli and spirochætæ in greater or less numbers, and that one-third of the cases will have them in preponderating numbers. This is a somewhat higher rate than we have ever seen reported in temperate climates. However, it must be remembered that in all of the cases examined we were on the lookout for these particular parasites. The associated spirochætæ and fusiform bacilli have been found in an ulcer of the skin and in 2 cases of pulmonary disease, but as yet there is no evidence to show that in the Philippines they are common in these situations.

One caution needs to be given. In our opinion the finding of fusiform bacilli and spirochætæ in a throat lesion does not justify one in resting content with a diagnosis of "Vincent's Angina." Experience shows that syphilis, diphtheria, carcinoma, (and very probably other etiologic factors) must be carefully ruled out. It is still an open question whether the associated fusiform bacilli and spirochætæ are ever causative of the multifiform lesions in which they are so often found to be present.

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## ILLUSTRATIONS.

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### PLATE I.

FIGS. 1 and 2. Spirochætæ and fusiform bacilli in smears from an ulcer of the tonsil.

FIG. 3. Spirochætæ and fusiform bacilli in a smear from an ulcer of the tonsil, showing beaded staining.

### PLATE II.

FIG. 4. Spirochætæ and fusiform bacilli in a smear from an ulcer of the gums.

FIGS. 5 and 6. Spirochætæ and fusiform bacilli in smears from an ulcer of the foot.

Magnification in all figures 1,000 diameters. Photomicrographs by Mr. Charles Martin of the Bureau of Science, Manila.





Fig. 1.



Fig. 2.



Fig. 3.







Fig. 4.

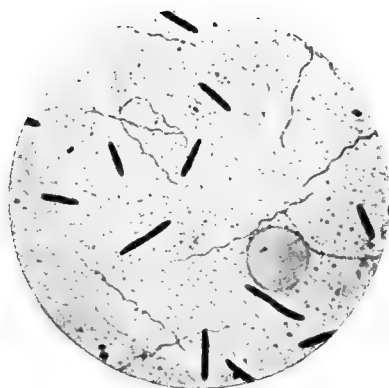


Fig. 5.

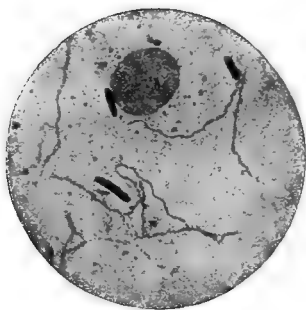


Fig. 6.

PLATE II.



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